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> O <
O|  |O  IntelliGenetics
> O <

Quest - Quick User-directed Expression Search Tool
Release 5.4

                -- Outline of search "cterm_spt" --

Selected search type is key against sequence data banks or files.
Selected scope is Sequence.
Selected sequence key from "kam547.key":
  cterm (AA) ID   cterm AA preliminary pattern
1       hfrw

Selected files:

        File : ctermspt.pep

                      -- Output Parameters --

Format Options:                         File Options:
  Nucleic acid code matching   Exact     Indirect file                 No
  Find non-matching hits only  No        Sequence or key file          No
  Report key used              Yes       List of hits                  Yes
  Note position of hit         Yes       Hit display                   Yes
  Display full annotations     Yes       Name and annotations          Yes
  Sequence context             50


                      -- Run Parameters --

  Run mode                     Batch
    Time to start comparison   now
    Notify at end of run       No

-------
1 match found in sequence:
 q8cwu6 ; 30S ribosomal protein S7.
  (from "ctermspt.pep")
  TOIG of: q8cwu6  check: 790  from: 1  to: 156

 ID   Q8CWU6      PRELIMINARY;      PRT;   156 AA.
 AC   Q8CWU6;
 DT   01-MAR-2003 (TrEMBLrel. 23, Created)
 DT   01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
 DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
 DE   30S ribosomal protein S7.
 GN   RPSG OR SPR0249.
 OS   Streptococcus pneumoniae (strain ATCC BAA-255 / R6).
 OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
 OC   Streptococcus.
 OX   NCBI_TaxID=171101;
 RN   [1]
 RP   SEQUENCE FROM N.A.
 RX   MEDLINE=21429245; PubMed=11544234;
 RA   Hoskins J., Alborn W.E. Jr., Arnold J., Blaszczak L.C., Burgett S.,
 RA   DeHoff B.S., Estrem S.T., Fritz L., Fu D.-J., Fuller W., Geringer C.,
 RA   Gilmour R., Glass J.S., Khoja H., Kraft A.R., Lagace R.E.,
 RA   LeBlanc D.J., Lee L.N., Lefkowitz E.J., Lu J., Matsushima P.,
 RA   McAhren S.M., McHenney M., McLeaster K., Mundy C.W., Nicas T.I.,
 RA   Norris F.H., O'Gara M., Peery R.B., Robertson G.T., Rockey P.,
 RA   Sun P.-M., Winkler M.E., Yang Y., Young-Bellido M., Zhao G.,
 RA   Zook C.A., Baltz R.H., Jaskunas S.R., Rosteck P.R. Jr., Skatrud P.L.,
 RA   Glass J.I.;
 RT   "Genome of the bacterium Streptococcus pneumoniae strain R6.";
 RL   J. Bacteriol. 183:5709-5717(2001).
 DR   EMBL; AE008406; AAK99053.1; -.
 KW   Complete proteome.
 SQ   SEQUENCE   156 AA;  17756 MW;  877FAB5C7DC7D2B8 CRC64;

  Q8CWU6  Length: 156  September 17, 2003 13:10  Type: P  Check: 790  ..
 Found using 'cterm' (kam547.key)

...

                                                                      |--|
103     WLVTIARLRGEHTMQDRLAKEILDAANNTGAAVKKREDTHRMAEANRAFAHFRW
                                                                      153

-------
1 match found in sequence:
 q8dvv5 ; 30S ribosomal protein S7.
  (from "ctermspt.pep")
  TOIG of: q8dvv5  check: 1800  from: 1  to: 156

 ID   Q8DVV5      PRELIMINARY;      PRT;   156 AA.
 AC   Q8DVV5;
 DT   01-MAR-2003 (TrEMBLrel. 23, Created)
 DT   01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
 DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
 DE   30S ribosomal protein S7.
 GN   SMU.358.
 OS   Streptococcus mutans.
 OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
 OC   Streptococcus.
 OX   NCBI_TaxID=1309;
 RN   [1]
 RP   SEQUENCE FROM N.A.
 RC   STRAIN=UA159 / ATCC 700610 / Serotype C;
 RX   MEDLINE=22295063; PubMed=12397186;
 RA   Ajdic D., McShan W.M., McLaughlin R.E., Savic G., Chang J.,
 RA   Carson M.B., Primeaux C., Tian R., Kenton S., Jia H., Lin S., Qian Y.,
 RA   Li S., Zhu H., Najar F., Lai H., White J., Roe B.A., Ferretti J.J.;
 RT   "Genome sequence of Streptococcus mutans UA159, a cariogenic dental
 RT   pathogen.";
 RL   Proc. Natl. Acad. Sci. U.S.A. 99:14434-14439(2002).
 DR   EMBL; AE014883; AAN58116.1; -.
 KW   Ribosomal protein; Complete proteome.
 SQ   SEQUENCE   156 AA;  17805 MW;  714CF68821CF1BFB CRC64;

 Q8DVV5  Length: 156  September 17, 2003 13:10  Type: P  Check: 1800  ..
 Found using 'cterm' (kam547.key)

...

                                                                      |--|
103     WLVTASRTRGEHTMKDRLAKEILDASNNTGASVKKREDTHRMAEANRAFAHFRW
                                                                      153

-------
1 match found in sequence:
 q8dxs6 ; Ribosomal protein S7.
  (from "ctermspt.pep")
  TOIG of: q8dxs6  check: 9852  from: 1  to: 156

 ID   Q8DXS6      PRELIMINARY;      PRT;   156 AA.
 AC   Q8DXS6;
 DT   01-MAR-2003 (TrEMBLrel. 23, Created)
 DT   01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
 DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
 DE   Ribosomal protein S7.
 GN   RPSG OR SAG1770.
 OS   Streptococcus agalactiae (serotype V).
 OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
 OC   Streptococcus.
 OX   NCBI_TaxID=216466;
 RN   [1]
 RP   SEQUENCE FROM N.A.
 RC   STRAIN=2603 V/R / Serotype V;
 RX   MEDLINE=22222988; PubMed=12200547;
 RA   Tettelin H., Masignani V., Cieslewicz M.J., Eisen J.A., Peterson S.,
 RA   Wessels M.R., Paulsen I.T., Nelson K.E., Margarit I., Read T.D.,
 RA   Madoff L.C., Wolf A.M., Beanan M.J., Brinkac L.M., Daugherty S.C.,
 RA   DeBoy R.T., Durkin A.S., Kolonay J.F., Madupu R., Lewis M.R.,
 RA   Radune D., Fedorova N.B., Scanlan D., Khouri H., Mulligan S.,
```

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RA   Carty H.A., Cline R.T., Van Aken S.E., Gill J., Scarselli M., Mora M.,
RA   Iacobini E.T., Brettoni C., Galli G., Mariani M., Vegni F., Maione D.,
RA   Rinaudo D., Rappuoli R., Telford J.L., Kasper D.L., Grandi G.,
RA   Fraser C.M.;
RT   "Complete genome sequence and comparative genomic analysis of an
RT   emerging human pathogen, serotype V Streptococcus agalactiae.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:12391-12396(2002).
DR   EMBL; AE014272; AAN00633.1; -.
DR   TIGR; SAG1770; -.
KW   Complete proteome.
SQ   SEQUENCE   156 AA;  17695 MW;  7285E9860F4E983B CRC64;

Q8DXS6  Length: 156  September 17, 2003 13:10  Type: P  Check: 9852  ..
Found using 'cterm' (kam547.key)

...

                                                                |--|
103     WLVNASRARGEHTMKDRLAKEIMDAANNTGASVKKREDTHKMAEANRAFAHFRW
                                                                153

-------
1 match found in sequence:
q8e3e6 ; Ribosomal protein S7.
  (from "ctermspt.pep")
  TOIG of: q8e3e6  check: 9852  from: 1  to: 156

ID   Q8E3E6      PRELIMINARY;      PRT;   156 AA.
AC   Q8E3E6;
DT   01-MAR-2003 (TrEMBLrel. 23, Created)
DT   01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   Ribosomal protein S7.
GN   RPSG OR GBS1813.
OS   Streptococcus agalactiae (serotype III).
OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
OC   Streptococcus.
OX   NCBI_TaxID=216495;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=NEM316 / Serotype III;
RX   MEDLINE=22242508; PubMed=12354221;
RA   Glaser P., Rusniok C., Buchrieser C., Chevalier F., Frangeul L.,
RA   Msadek T., Zouine M., Couve E., Lalioui L., Poyart C., Trieu-Cuot P.,
RA   Kunst F.;
RT   "Genome sequence of Streptococcus agalactiae, a pathogen causing
RT   invasive neonatal disease.";
RL   Mol. Microbiol. 45:1499-1513(2002).
DR   EMBL; AL766853; CAD47472.1; -.
DR   SagaList; gbs1813; -.
KW   Complete proteome.
SQ   SEQUENCE   156 AA;  17695 MW;  7285E9860F4E983B CRC64;

Q8E3E6  Length: 156  September 17, 2003 13:10  Type: P  Check: 9852  ..
Found using 'cterm' (kam547.key)

...

                                                                |--|
103     WLVNASRARGEHTMKDRLAKEIMDAANNTGASVKKREDTHKMAEANRAFAHFRW
                                                                153

-------
1 match found in sequence:
q9mg88 ; Ribosomal protein S7.
  (from "ctermspt.pep")
  TOIG of: q9mg88  check: 3686  from: 1  to: 162

ID   Q9MG88      PRELIMINARY;      PRT;   162 AA.
AC   Q9MG88;
DT   01-OCT-2000 (TrEMBLrel. 15, Created)
DT   01-OCT-2000 (TrEMBLrel. 15, Last sequence update)
DT   01-DEC-2001 (TrEMBLrel. 19, Last annotation update)
DE   Ribosomal protein S7.
GN   RPS7.
OS   Chrysodidymus synuroideus.
OG   Mitochondrion.
OC   Eukaryota; stramenopiles; Chrysophyceae; Synurales; Chrysodidymus.
OX   NCBI_TaxID=47573;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=20330374; PubMed=10871400;
RA   Chesnick J.M., Goff M., Graham J., Ocampo C., Lang B.F., Seif E.,
RA   Burger G.;
RT   "The mitochondrial genome of the stramenopile alga Chrysodidymus
RT   synuroideus. Complete sequence, gene content and genome
RT   organization.";
RL   Nucleic Acids Res. 28:2512-2518(2000).
RN   [2]
RP   SEQUENCE FROM N.A.
RA   Burger G.;
RL   Submitted (JAN-2000) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF222718; AAF36961.1; -.
KW   Mitochondrion.
SQ   SEQUENCE   162 AA;  19370 MW;  0FDEB8142AE6D1EC CRC64;

Q9MG88  Length: 162  September 17, 2003 13:10  Type: P  Check: 3686  ..
Found using 'cterm' (kam547.key)

...

                                                                    |--|
109     ETLILDKRKISFGEKLRHEIFLLLSKEKLSKSLQLKKDNLLKAAQNRSNVHFRW
                                                                    159


                        -- Search Statistics --

Times:                      CPU                    Total Elapsed
                         00:00:00.00               00:00:00.00

Number of sequences searched:                          5
Number of sequence hits:                               5
Number of separate matches:                            5
Number of sequence hits saved:                         0
```

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> O <
O| |O  IntelliGenetics
> O <

Quest - Quick User-directed Expression Search Tool
Release 5.4

                -- Outline of search "cterm_sp" --

Selected search type is key against sequence data banks or files.
Selected scope is Sequence.
Selected sequence key from "kam547.key":
  cterm (AA) ID   cterm AA preliminary pattern
1       hfrw

Selected files:

        File : ctermsp.pep

                    -- Output Parameters --

Format Options:                     File Options:
  Nucleic acid code matching  Exact   Indirect file              No
  Find non-matching hits only No      Sequence or key file      No
  Report key used             Yes     List of hits              Yes
  Note position of hit        Yes     Hit display               Yes
  Display full annotations    Yes     Name and annotations      Yes
  Sequence context            50


                    -- Run Parameters --

  Run mode                    Batch
    Time to start comparison  now
    Notify at end of run      No

-------
1 match found in sequence:
 rs7lacla ; 30S ribosomal protein S7.
  (from "ctermsp.pep")
  TOIG of: rs7_lacla  check: 8558  from: 1  to: 155

 ID   RS7_LACLA      STANDARD;      PRT;   155 AA.
 AC   Q9CDG0;
 DT   28-FEB-2003 (Rel. 41, Created)
 DT   28-FEB-2003 (Rel. 41, Last sequence update)
 DT   28-FEB-2003 (Rel. 41, Last annotation update)
 DE   30S ribosomal protein S7.
 GN   RPSG OR LL2261.
 OS   Lactococcus lactis (subsp. lactis) (Streptococcus lactis).
 OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae; Lactococcus.
 OX   NCBI_TaxID=1360;
 RN   [1]
 RP   SEQUENCE FROM N.A.
 RC   STRAIN=IL1403;
 RX   MEDLINE=21235186; PubMed=11337471;
 RA   Bolotin A., Wincker P., Mauger S., Jaillon O., Malarme K.,
 RA   Weissenbach J., Ehrlich S.D., Sorokin A.;
 RT   "The complete genome sequence of the lactic acid bacterium Lactococcus
 RT   lactis ssp. lactis IL1403.";
 RL   Genome Res. 11:731-753(2001).
 CC   -!- FUNCTION: One of the primary rRNA binding proteins, it binds
 CC       directly to 16S rRNA where it nucleates assembly of the head
 CC       domain of the 30S subunit. Is located at the subunit interface
 CC       close to the decoding center, probably blocks exit of the E-site
 CC       tRNA (By similarity).
 CC   -!- SUBUNIT: Part of the 30S ribosomal subunit. Contacts proteins S9
 CC       and S11 (By similarity).
 CC   -!- SIMILARITY: BELONGS TO THE S7P FAMILY OF RIBOSOMAL PROTEINS.
 CC   ----------------------------------------------------------------------
 CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC   the European Bioinformatics Institute. There are no restrictions on its
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 CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
 CC   or send an email to license@isb-sib.ch).
 CC   ----------------------------------------------------------------------
 DR   EMBL; AE006455; AAK06359.1; -.
 DR   PIR; E86907; E86907.
 DR   HSSP; P22744; 1HUS.
 DR   HAMAP; MF_00480; -; 1.
 DR   InterPro; IPR000235; Ribosomal_S7.
 DR   InterPro; IPR005717; S7_bact_org.
 DR   Pfam; PF00177; Ribosomal_S7; 1.
 DR   ProDom; PD000817; Ribosomal_S7; 1.
 DR   TIGRFAMs; TIGR01029; rpsG_bact; 1.
 DR   PROSITE; PS00052; RIBOSOMAL_S7; 1.
 KW   Ribosomal protein; RNA-binding; rRNA-binding; tRNA-binding;
 KW   Complete proteome.
 SQ   SEQUENCE   155 AA;  17683 MW;  650E15C1A25CA99B CRC64;

 RS7_LACLA  Length: 155  September 17, 2003 13:10  Type: P  Check: 8558  ..
 Found using 'cterm' (kam547.key)

...

                                                                    |--|
102     WLVTIARNRGEHTMQDRLAKEILDAANNTGAAVKKREDTHKMAEANRAFAHFRW
                                                                   152

-------
1 match found in sequence:
 rs7mycpu ; 30S ribosomal protein S7.
  (from "ctermsp.pep")
  TOIG of: rs7_mycpu  check: 2961  from: 1  to: 156

 ID   RS7_MYCPU      STANDARD;      PRT;   156 AA.
 AC   Q98QD7;
 DT   28-FEB-2003 (Rel. 41, Created)
 DT   28-FEB-2003 (Rel. 41, Last sequence update)
 DT   28-FEB-2003 (Rel. 41, Last annotation update)
 DE   30S ribosomal protein S7.
 GN   RPSG OR MYPU_4290.
 OS   Mycoplasma pulmonis.
 OC   Bacteria; Firmicutes; Mollicutes; Mycoplasmataceae; Mycoplasma.
 OX   NCBI_TaxID=2107;
 RN   [1]
 RP   SEQUENCE FROM N.A.
 RC   STRAIN=UAB CTIP;
 RX   MEDLINE=21267165; PubMed=11353084;
 RA   Chambaud I., Heilig R., Ferris S., Barbe V., Samson D., Galisson F.,
 RA   Moszer I., Dybvig K., Wroblewski H., Viari A., Rocha E.P.C.,
 RA   Blanchard A.;
 RT   "The complete genome sequence of the murine respiratory pathogen
 RT   Mycoplasma pulmonis.";
 RL   Nucleic Acids Res. 29:2145-2153(2001).
 CC   -!- FUNCTION: One of the primary rRNA binding proteins, it binds
 CC       directly to 16S rRNA where it nucleates assembly of the head
 CC       domain of the 30S subunit. Is located at the subunit interface
 CC       close to the decoding center, probably blocks exit of the E-site
 CC       tRNA (By similarity).
 CC   -!- SUBUNIT: Part of the 30S ribosomal subunit. Contacts proteins S9
 CC       and S11 (By similarity).
 CC   -!- SIMILARITY: BELONGS TO THE S7P FAMILY OF RIBOSOMAL PROTEINS.
 CC   ----------------------------------------------------------------------
 CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
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 CC   modified and this statement is not removed. Usage by and for commercial
 CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
 CC   or send an email to license@isb-sib.ch).
 CC   ----------------------------------------------------------------------
 DR   EMBL; AL445564; CAC13602.1; -.
 DR   PIR; E90565; E90565.
```

```
DR   MypuList; MYPU_4290; -.
DR   HAMAP; MF_00480; -; 1.
DR   InterPro; IPR000235; Ribosomal_S7.
DR   InterPro; IPR005717; S7_bact_org.
DR   Pfam; PF00177; Ribosomal_S7; 1.
DR   ProDom; PD000817; Ribosomal_S7; 1.
DR   TIGRFAMs; TIGR01029; rpsG_bact; 1.
DR   PROSITE; PS00052; RIBOSOMAL_S7; FALSE_NEG.
KW   Ribosomal protein; RNA-binding; rRNA-binding; tRNA-binding;
KW   Complete proteome.
SQ   SEQUENCE   156 AA;  18015 MW;  3C464EEC7DD3FC98 CRC64;

RS7_MYCPU  Length: 156  September 17, 2003 13:10  Type: P  Check: 2961  ..
Found using 'cterm' (kam547.key)

...

                                                                |--|
103     WLTNYARLRNEKTMDLRLANEIIDASNKTGGAIKKREDTHKMAEANRAFAHFRW
                                                               153

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1 match found in sequence:
rs7strp3 ; 30S ribosomal protein S7.
 (from "ctermsp.pep")
 TOIG of: rs7_strp3  check: 178  from: 1  to: 156

ID   RS7_STRP3      STANDARD;      PRT;   156 AA.
AC   P59062;
DT   28-FEB-2003 (Rel. 41, Created)
DT   28-FEB-2003 (Rel. 41, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   30S ribosomal protein S7.
GN   RPSG OR SPYM3_0199 OR SPS0204.
OS   Streptococcus pyogenes (serotype M3).
OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
OC   Streptococcus.
OX   NCBI_TaxID=198466;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=MGAS315 / Serotype M3;
RX   MEDLINE=22133808; PubMed=12122206;
RA   Beres S.B., Sylva G.L., Barbian K.D., Lei B., Hoff J.S.,
RA   Mammarella N.D., Liu M.-Y., Smoot J.C., Porcella S.F., Parkins L.D.,
RA   Campbell D.S., Smith T.M., McCormick J.K., Leung D.Y.M.,
RA   Schlievert P.M., Musser J.M.;
RT   "Genome sequence of a serotype M3 strain of group A Streptococcus:
RT   phage-encoded toxins, the high-virulence phenotype, and clone
RT   emergence.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:10078-10083(2002).
RN   [2]
RP   SEQUENCE FROM N.A.
RC   STRAIN=SSI-1 / Serotype M3;
RA   Nakagawa I., Kurokawa K., Nakata M., Tomiyasu Y., Yamashita A.,
RA   Yamazaki K., Okahashi N., Kawabata S., Yasunaga T., Hattori M.,
RA   Hayashi H., Hamada S.;
RT   "The genome of invasive Streptococcus pyogenes; a comparative analysis
RT   of S. pyogenes SSI-1, SF370 and MGAS8232.";
RL   Submitted (MAY-2002) to the EMBL/GenBank/DDBJ databases.
CC   -!- FUNCTION: One of the primary rRNA binding proteins, it binds
CC       directly to 16S rRNA where it nucleates assembly of the head
CC       domain of the 30S subunit. Is located at the subunit interface
CC       close to the decoding center, probably blocks exit of the E-site
CC       tRNA (By similarity).
CC   -!- SUBUNIT: Part of the 30S ribosomal subunit. Contacts proteins S9
CC       and S11 (By similarity).
CC   -!- SIMILARITY: BELONGS TO THE S7P FAMILY OF RIBOSOMAL PROTEINS.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; AE014140; AAM78806.1; -.
DR   EMBL; AP005141; BAC63299.1; -.
DR   HAMAP; MF_00480; -; 1.
DR   InterPro; IPR000235; Ribosomal_S7.
DR   InterPro; IPR005717; S7_bact_org.
DR   Pfam; PF00177; Ribosomal_S7; 1.
DR   ProDom; PD000817; Ribosomal_S7; 1.
DR   TIGRFAMs; TIGR01029; rpsG_bact; 1.
DR   PROSITE; PS00052; RIBOSOMAL_S7; 1.
KW   Ribosomal protein; RNA-binding; rRNA-binding; tRNA-binding;
KW   Complete proteome.
SQ   SEQUENCE   156 AA;  17652 MW;  ACFD1ADB39155166 CRC64;

RS7_STRP3  Length: 156  September 17, 2003 13:10  Type: P  Check: 178  ..
Found using 'cterm' (kam547.key)

...

                                                                |--|
103     WLVNASRARGEHTMKDRLAKEIMDAANNTGASVKKREDTHKMAEANRAFAHFRW
                                                               153

-------
1 match found in sequence:
rs7strpn ; 30S ribosomal protein S7.
 (from "ctermsp.pep")
 TOIG of: rs7_strpn  check: 988  from: 1  to: 156

ID   RS7_STRPN      STANDARD;      PRT;   156 AA.
AC   Q97SQ4;
DT   28-FEB-2003 (Rel. 41, Created)
DT   28-FEB-2003 (Rel. 41, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   30S ribosomal protein S7.
GN   RPSG OR SP0272.
OS   Streptococcus pneumoniae.
OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
OC   Streptococcus.
OX   NCBI_TaxID=1313;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=ATCC BAA-334 / TIGR4;
RX   MEDLINE=21357209; PubMed=11463916;
RA   Tettelin H., Nelson K.E., Paulsen I.T., Eisen J.A., Read T.D.,
RA   Peterson S., Heidelberg J., DeBoy R.T., Haft D.H., Dodson R.J.,
RA   Durkin A.S., Gwinn M., Kolonay J.F., Nelson W.C., Peterson J.D.,
RA   Umayam L.A., White O., Salzberg S.L., Lewis M.R., Radune D.,
RA   Holtzapple E., Khouri H., Wolf A.M., Utterback T.R., Hansen C.L.,
RA   McDonald L.A., Feldblyum T.V., Angiuoli S., Dickinson T., Hickey E.K.,
RA   Holt I.E., Loftus B.J., Yang F., Smith H.O., Venter J.C.,
RA   Dougherty B.A., Morrison D.A., Hollingshead S.K., Fraser C.M.;
RT   "Complete genome sequence of a virulent isolate of Streptococcus
RT   pneumoniae.";
RL   Science 293:498-506(2001).
CC   -!- FUNCTION: One of the primary rRNA binding proteins, it binds
CC       directly to 16S rRNA where it nucleates assembly of the head
CC       domain of the 30S subunit. Is located at the subunit interface
CC       close to the decoding center, probably blocks exit of the E-site
CC       tRNA (By similarity).
CC   -!- SUBUNIT: Part of the 30S ribosomal subunit. Contacts proteins S9
CC       and S11 (By similarity).
CC   -!- SIMILARITY: BELONGS TO THE S7P FAMILY OF RIBOSOMAL PROTEINS.
CC   ----------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
```

```
CC   ----------------------------------------------------------------------
DR   EMBL; AE007340; AAK74450.1; -.
DR   PIR; A95032; A95032.
DR   TIGR; SP0272; -.
DR   HAMAP; MF_00480; -; 1.
DR   InterPro; IPR000235; Ribosomal_S7.
DR   InterPro; IPR005717; S7_bact_org.
DR   Pfam; PF00177; Ribosomal_S7; 1.
DR   ProDom; PD000817; Ribosomal_S7; 1.
DR   TIGRFAMs; TIGR01029; rpsG_bact; 1.
DR   PROSITE; PS00052; RIBOSOMAL_S7; 1.
KW   Ribosomal protein; RNA-binding; rRNA-binding; tRNA-binding;
KW   Complete proteome.
SQ   SEQUENCE   156 AA;  17755 MW;  877FA3745DCFFA98 CRC64;

RS7_STRPN  Length: 156  September 17, 2003 13:10  Type: P  Check: 988  ..
Found using 'cterm' (kam547.key)

...

                                                                    |--|
103     WLVTIARLRGEHTMQDRLAKEILDAANNTGAAVKKREDTHRMAEANRAFAHFRW
                                                                   153

-------
1 match found in sequence:
 rs7strpy ; 30S ribosomal protein S7.
  (from "ctermsp.pep")
  TOIG of: rs7_strpy  check: 9938  from: 1  to: 156

 ID   RS7_STRPY      STANDARD;      PRT;   156 AA.
 AC   Q9A1H2;
 DT   28-FEB-2003 (Rel. 41, Created)
 DT   28-FEB-2003 (Rel. 41, Last sequence update)
 DT   28-FEB-2003 (Rel. 41, Last annotation update)
 DE   30S ribosomal protein S7.
 GN   RPSG OR SPY0272 OR SPYM18_0259.
 OS   Streptococcus pyogenes, and
 OS   Streptococcus pyogenes (serotype M18).
 OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
 OC   Streptococcus.
 OX   NCBI_TaxID=1314, 186103;
 RN   [1]
 RP   SEQUENCE FROM N.A.
 RC   STRAIN=SF370 / ATCC 700294 / Serotype M1;
 RX   MEDLINE=21192684; PubMed=11296296;
 RA   Ferretti J.J., McShan W.M., Ajdic D.J., Savic D.J., Savic G., Lyon K.,
 RA   Primeaux C., Sezate S., Suvorov A.N., Kenton S., Lai H.S., Lin S.P.,
 RA   Qian Y., Jia H.G., Najar F.Z., Ren Q., Zhu H., Song L., White J.,
 RA   Yuan X., Clifton S.W., Roe B.A., McLaughlin R.;
 RT   "Complete genome sequence of an M1 strain of Streptococcus pyogenes.";
 RL   Proc. Natl. Acad. Sci. U.S.A. 98:4658-4663(2001).
 RN   [2]
 RP   SEQUENCE FROM N.A.
 RC   STRAIN=MGAS8232 / Serotype M18;
 RX   MEDLINE=21927593; PubMed=11917108;
 RA   Smoot J.C., Barbian K.D., Van Gompel J.J., Smoot L.M., Chaussee M.S.,
 RA   Sylva G.L., Sturdevant D.E., Ricklefs S.M., Porcella S.F.,
 RA   Parkins L.D., Beres S.B., Campbell D.S., Smith T.M., Zhang Q.,
 RA   Kapur V., Daly J.A., Veasy L.G., Musser J.M.;
 RT   "Genome sequence and comparative microarray analysis of serotype M18
 RT   group A Streptococcus strains associated with acute rheumatic fever
 RT   outbreaks.";
 RL   Proc. Natl. Acad. Sci. U.S.A. 99:4668-4673(2002).
 CC   -!- FUNCTION: One of the primary rRNA binding proteins, it binds
 CC       directly to 16S rRNA where it nucleates assembly of the head
 CC       domain of the 30S subunit. Is located at the subunit interface
 CC       close to the decoding center, probably blocks exit of the E-site
 CC       tRNA (By similarity).
 CC   -!- SUBUNIT: Part of the 30S ribosomal subunit. Contacts proteins S9
 CC       and S11 (By similarity).
 CC   -!- SIMILARITY: BELONGS TO THE S7P FAMILY OF RIBOSOMAL PROTEINS.
 CC   ----------------------------------------------------------------------
 CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
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 CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
 CC   or send an email to license@isb-sib.ch).
 CC   ----------------------------------------------------------------------
 DR   EMBL; AE006493; AAK33346.1; -.
 DR   EMBL; AE009973; AAL97039.1; -.
 DR   HSSP; P22744; 1HUS.
 DR   HAMAP; MF_00480; -; 1.
 DR   InterPro; IPR000235; Ribosomal_S7.
 DR   InterPro; IPR005717; S7_bact_org.
 DR   Pfam; PF00177; Ribosomal_S7; 1.
 DR   ProDom; PD000817; Ribosomal_S7; 1.
 DR   TIGRFAMs; TIGR01029; rpsG_bact; 1.
 DR   PROSITE; PS00052; RIBOSOMAL_S7; 1.
 KW   Ribosomal protein; RNA-binding; rRNA-binding; tRNA-binding;
 KW   Complete proteome.
 SQ   SEQUENCE   156 AA;  17679 MW;  9790B8921284F3EC CRC64;

 RS7_STRPY  Length: 156  September 17, 2003 13:10  Type: P  Check: 9938  ..
 Found using 'cterm' (kam547.key)

 ...

                                                                    |--|
 103     WLVNASRARGEHTMKDRLAKEIMDAANNTGASVKKREDTHKMAEANRAFAHFRW
                                                                   153

 -------
 1 match found in sequence:
  rs7aaquae ; 30S ribosomal protein S7-1.
   (from "ctermsp.pep")
   TOIG of: rs7a_aquae  check: 4582  from: 1  to: 160

  ID   RS7A_AQUAE     STANDARD;      PRT;   160 AA.
  AC   O67690;
  DT   30-MAY-2000 (Rel. 39, Created)
  DT   30-MAY-2000 (Rel. 39, Last sequence update)
  DT   28-FEB-2003 (Rel. 41, Last annotation update)
  DE   30S ribosomal protein S7-1.
  GN   RPSG1 OR AQ_1832.
  OS   Aquifex aeolicus.
  OC   Bacteria; Aquificae; Aquificales; Aquificaceae; Aquifex.
  OX   NCBI_TaxID=63363;
  RN   [1]
  RP   SEQUENCE FROM N.A.
  RC   STRAIN=VF5;
  RX   MEDLINE=98196666; PubMed=9537320;
  RA   Deckert G., Warren P.V., Gaasterland T., Young W.G., Lenox A.L.,
  RA   Graham D.E., Overbeek R., Snead M.A., Keller M., Aujay M., Huber R.,
  RA   Feldman R.A., Short J.M., Olson G.J., Swanson R.V.;
  RT   "The complete genome of the hyperthermophilic bacterium Aquifex
  RT   aeolicus.";
  RL   Nature 392:353-358(1998).
  CC   -!- FUNCTION: One of the primary rRNA binding proteins, it binds
  CC       directly to 16S rRNA where it nucleates assembly of the head
  CC       domain of the 30S subunit. Is located at the subunit interface
  CC       close to the decoding center, probably blocks exit of the E-site
  CC       tRNA (By similarity).
  CC   -!- SUBUNIT: Part of the 30S ribosomal subunit. Contacts proteins S9
  CC       and S11 (By similarity).
  CC   -!- SIMILARITY: BELONGS TO THE S7P FAMILY OF RIBOSOMAL PROTEINS.
  CC   ----------------------------------------------------------------------
  CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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  CC   the European Bioinformatics Institute. There are no restrictions on its
  CC   use by non-profit institutions as long as its content is in no way
  CC   modified and this statement is not removed. Usage by and for commercial
  CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
  CC   or send an email to license@isb-sib.ch).
```

```
CC   ----------------------------------------------------------------------
DR   EMBL; AE000758; AAC07654.1; -.
DR   PIR; G70457; G70457.
DR   HSSP; P17291; 1RSS.
DR   HAMAP; MF_00480; -; 1.
DR   InterPro; IPR000235; Ribosomal_S7.
DR   InterPro; IPR005717; S7_bact_org.
DR   Pfam; PF00177; Ribosomal_S7; 1.
DR   ProDom; PD000817; Ribosomal_S7; 1.
DR   TIGRFAMs; TIGR01029; rpsG_bact; 1.
DR   PROSITE; PS00052; RIBOSOMAL_S7; 1.
KW   Ribosomal protein; RNA-binding; rRNA-binding; tRNA-binding;
KW   Complete proteome.
SQ   SEQUENCE   160 AA;  18625 MW;  B93333A12182B3F1 CRC64;

RS7A_AQUAE  Length: 160  September 17, 2003 13:10  Type: P  Check: 4582  ..
Found using 'cterm' (kam547.key)

...

                                                              |--|
107     AARERPRGREQYTMIERLKAELLDALNERGGAYKKKEETHRMAHANMVFSHFRW
                                                            157

-------
1 match found in sequence:
 rs7baquae ; 30S ribosomal protein S7-2.
  (from "ctermsp.pep")
  TOIG of: rs7b_aquae  check: 4544  from: 1  to: 160

 ID   RS7B_AQUAE     STANDARD;      PRT;   160 AA.
 AC   O66944;
 DT   30-MAY-2000 (Rel. 39, Created)
 DT   30-MAY-2000 (Rel. 39, Last sequence update)
 DT   28-FEB-2003 (Rel. 41, Last annotation update)
 DE   30S ribosomal protein S7-2.
 GN   RPSG2 OR AQ_734.
 OS   Aquifex aeolicus.
 OC   Bacteria; Aquificae; Aquificales; Aquificaceae; Aquifex.
 OX   NCBI_TaxID=63363;
 RN   [1]
 RP   SEQUENCE FROM N.A.
 RC   STRAIN=VF5;
 RX   MEDLINE=98196666; PubMed=9537320;
 RA   Deckert G., Warren P.V., Gaasterland T., Young W.G., Lenox A.L.,
 RA   Graham D.E., Overbeek R., Snead M.A., Keller M., Aujay M., Huber R.,
 RA   Feldman R.A., Short J.M., Olson G.J., Swanson R.V.;
 RT   "The complete genome of the hyperthermophilic bacterium Aquifex
 RT   aeolicus.";
 RL   Nature 392:353-358(1998).
 CC   -!- FUNCTION: One of the primary rRNA binding proteins, it binds
 CC       directly to 16S rRNA where it nucleates assembly of the head
 CC       domain of the 30S subunit. Is located at the subunit interface
 CC       close to the decoding center, probably blocks exit of the E-site
 CC       tRNA (By similarity).
 CC   -!- SUBUNIT: Part of the 30S ribosomal subunit. Contacts proteins S9
 CC       and S11 (By similarity).
 CC   -!- SIMILARITY: BELONGS TO THE S7P FAMILY OF RIBOSOMAL PROTEINS.
 CC   ----------------------------------------------------------------------
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 CC   modified and this statement is not removed. Usage by and for commercial
 CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
 CC   or send an email to license@isb-sib.ch).
 CC   ----------------------------------------------------------------------
 DR   EMBL; AE000705; AAC06909.1; -.
 DR   PIR; D70364; D70364.
 DR   HSSP; P17291; 1RSS.
 DR   HAMAP; MF_00480; -; 1.
 DR   InterPro; IPR000235; Ribosomal_S7.
 DR   InterPro; IPR005717; S7_bact_org.
 DR   Pfam; PF00177; Ribosomal_S7; 1.
 DR   ProDom; PD000817; Ribosomal_S7; 1.
 DR   TIGRFAMs; TIGR01029; rpsG_bact; 1.
 DR   PROSITE; PS00052; RIBOSOMAL_S7; 1.
 KW   Ribosomal protein; RNA-binding; rRNA-binding; tRNA-binding;
 KW   Complete proteome.
 SQ   SEQUENCE   160 AA;  18608 MW;  8F33377ED804E620 CRC64;

 RS7B_AQUAE  Length: 160  September 17, 2003 13:10  Type: P  Check: 4544  ..
 Found using 'cterm' (kam547.key)

...

                                                              |--|
107     AARERPRGRGQYTMIERLKAELLDALNERGGAYKKKEETHRMAHANMVFSHFRW
                                                            157


                        -- Search Statistics --

Times:                    CPU                  Total Elapsed
                       00:00:00.00             00:00:01.00

Number of sequences searched:                        7
Number of sequence hits:                             7
Number of separate matches:                          7
Number of sequence hits saved:                       0
```

D70364 Length: 160 September 17, 2003 13:09 Type: P Check: 4544 ..
Found using 'cterm' (kam547.key)

...

```
                                                              |--|
107     AARERPRGRGQYTMIERLKAELLDALNERGGAYKKKEETHRMAHANMVFSHFRW
                                                             157
```

---
1 match found in sequence:
e86907 ; TOIG of: e86907 check: 8558 from: 1 to: 155
(from "ctermpir.pep")
TOIG of: e86907 check: 8558 from: 1 to: 155

P1;E86907 - 30S ribosomal protein S7 [imported] - Lactococcus lactis subsp. lactis (strain IL1403)
C;Species: Lactococcus lactis subsp. lactis
C;Date: 23-Mar-2001 #sequence_revision 23-Mar-2001 #text_change 03-Aug-2001
C;Accession: E86907
R;Bolotin, A.; Wincker, P.; Mauger, S.; Jaillon, O.; Malarme, K.; Weissenbach, J.; Ehrlich, S.D.; Sorokin, A.
Genome Res. 11, 731-753, 2001
A;Title: The complete genome sequence of the lactic acid bacterium Lactococcus lactis ssp. lactis IL1403.
A;Reference number: A86625; MUID:21235186; PMID:11337471
A;Accession: E86907
A;Status: preliminary
A;Molecule type: DNA
A;Residues: 1-155 <STO>
A;Cross-references: GB:AE005176; PID:g12725332; PIDN:AAK06359.1; GSPDB:GN00146
A;Experimental source: strain IL1403
C;Genetics:
A;Gene: rpsG
C;Superfamily: Escherichia coli ribosomal protein S7

E86907 Length: 155 September 17, 2003 13:09 Type: P Check: 8558 ..
Found using 'cterm' (kam547.key)

...

```
                                                              |--|
102     WLVTIARNRGEHTMQDRLAKEILDAANNTGAAVKKREDTHKMAEANRAFAHFRW
                                                             152
```

---
1 match found in sequence:
e90565 ; TOIG of: e90565 check: 2961 from: 1 to: 156
(from "ctermpir.pep")
TOIG of: e90565 check: 2961 from: 1 to: 156

P1;E90565 - 30S ribosomal protein S7 [imported] - Mycoplasma pulmonis (strain UAB CTIP)
C;Species: Mycoplasma pulmonis
C;Date: 24-May-2001 #sequence_revision 24-May-2001 #text_change 03-Aug-2001
C;Accession: E90565
R;Chambaud, I.; Heilig, R.; Ferris, S.; Barbe, V.; Samson, D.; Galisson, F.; Moszer, I.; Dybvig, K.; Wroblewski, H.; Viari, A.; Rocha, E.P.C.; Blanchard, A.
Nucleic Acids Res. 29, 2145-2153, 2001
A;Title: The complete genome sequence of the murine respiratory pathogen Mycoplasma pulmonis.
A;Reference number: A99512; MUID:21267165; PMID:11353084
A;Accession: E90565
A;Status: preliminary
A;Molecule type: DNA
A;Residues: 1-156 <KUR>
A;Cross-references: GB:AL445566; PID:g14089843; PIDN:CAC13602.1; GSPDB:GN00153
A;Experimental source: strain UAB CTIP
C;Genetics:
A;Gene: MYPU_4290
A;Genetic code: SGC3
C;Superfamily: Escherichia coli ribosomal protein S7

E90565 Length: 156 September 17, 2003 13:09 Type: P Check: 2961 ..
Found using 'cterm' (kam547.key)

...

```
                                                              |--|
103     WLTNYARLRNEKTMDLRLANEIIDASNKTGGAIKKREDTHKMAEANRAFAHFRW
                                                             153
```

---
1 match found in sequence:
g70457 ; TOIG of: g70457 check: 4582 from: 1 to: 160
(from "ctermpir.pep")
TOIG of: g70457 check: 4582 from: 1 to: 160

P1;G70457 - ribosomal protein S07 - Aquifex aeolicus
C;Species: Aquifex aeolicus
C;Date: 08-May-1998 #sequence_revision 08-May-1998 #text_change 13-Aug-1999
C;Accession: G70457
R;Deckert, G.; Warren, P.V.; Gaasterland, T.; Young, W.G.; Lenox, A.L.; Graham, D.E.; Overbeek, R.; Snead, M.A.; Keller, M.; Aujay, M.; Huber, R.; Feldman, R.A.; Short, J.M.; Olson, G.J.; Swanson, R.V.
Nature 392, 353-358, 1998
A;Title: The complete genome of the hyperthermophilic bacterium Aquifex aeolicus.
A;Reference number: A70300; MUID:98196666; PMID:9537320
A;Accession: G70457
A;Status: preliminary; nucleic acid sequence not shown; translation not shown
A;Molecule type: DNA
A;Residues: 1-160 <AQF>
A;Cross-references: GB:AE000758; NID:g2984111; PIDN:AAC07654.1; PID:g2984117; GB:AE000657
A;Experimental source: strain VF5
C;Genetics:
A;Gene: rpsG1
C;Superfamily: Escherichia coli ribosomal protein S7

G70457 Length: 160 September 17, 2003 13:09 Type: P Check: 4582 ..
Found using 'cterm' (kam547.key)

...

```
                                                              |--|
107     AARERPRGREQYTMIERLKAELLDALNERGGAYKKKEETHRMAHANMVFSHFRW
                                                             157
```

-- Search Statistics --

Times:	CPU	Total Elapsed
	00:00:00.00	00:00:01.00

Number of sequences searched:	6
Number of sequence hits:	6
Number of separate matches:	6
Number of sequence hits saved:	0

```
> O <
O| |O  IntelliGenetics
> O <

Quest - Quick User-directed Expression Search Tool
Release 5.4

                -- Outline of search "cterm_pir" --

Selected search type is key against sequence data banks or files.
Selected scope is Sequence.
Selected sequence key from "kam547.key":
  cterm (AA) ID   cterm AA preliminary pattern
1       hfrw

Selected files:

        File : ctermpir.pep

                        -- Output Parameters --

Format Options:                         File Options:
  Nucleic acid code matching   Exact     Indirect file                 No
  Find non-matching hits only  No        Sequence or key file          No
  Report key used              Yes       List of hits                  Yes
  Note position of hit         Yes       Hit display                   Yes
  Display full annotations     Yes       Name and annotations          Yes
  Sequence context             50


                        -- Run Parameters --

  Run mode                     Batch
    Time to start comparison   now
    Notify at end of run       No

-------
1 match found in sequence:
 a95032 ; TOIG of: a95032  check: 988  from: 1  to: 156
  (from "ctermpir.pep")
  TOIG of: a95032  check: 988  from: 1  to: 156

 P1;A95032 - ribosomal protein S7 [imported] - Streptococcus pneumoniae (strain
  TIGR4)
 C;Species: Streptococcus pneumoniae
 C;Date: 03-Aug-2001 #sequence_revision 03-Aug-2001 #text_change 24-Aug-2001
 C;Accession: A95032
 R;Tettelin, H.; Nelson, K.E.; Paulsen, I.T.; Eisen, J.A.; Read, T.D.; Peterson,
  S.; Heidelberg, J.; DeBoy, R.T.; Haft, D.H.; Dodson, R.J.; Durkin, A.S.; Gwinn,
  M.; Kolonay, J.F.; Nelson, W.C.; Peterson, J.D.; Umayam, L.A.; White, O.;
  Salzberg, S.L.; Lewis, M.R.; Radune, D.; Holtzapple, E.; Khouri, H.; Wolf,
  A.M.; Utterback, T.R.; Hansen, C.L.; McDonald, L.A.; Feldblyum, T.V.; Angiuoli,
  S.; Dickinson, T.; Hickey, E.K.; Holt, I.E.
 Science 293, 498-506, 2001
 A;Authors: Loftus, B.J.; Yang, F.; Smith, H.O.; Venter, J.C.; Dougherty, B.A.;
  Morrison, D.A.; Hollingshead, S.K.; Fraser, C.M.
 A;Title: Complete Genome Sequence of a virulent isolate of Streptococcus
  pneumoniae.
 A;Reference number: A95000; MUID:21357209; PMID:11463916
 A;Accession: A95032
 A;Status: preliminary
 A;Molecule type: DNA
 A;Residues: 1-156 <KUR>
 A;Cross-references: GB:AE005672; PIDN:AAK74450.1; PID:g14971743; GSPDB:GN00164;
  TIGR:SP4SP0272
 A;Experimental source: strain TIGR4
 C;Genetics:
 A;Gene: SP0272
 C;Superfamily: Escherichia coli ribosomal protein S7

  A95032  Length: 156  September 17, 2003 13:09  Type: P  Check: 988  ..
 Found using 'cterm' (kam547.key)

...

                                                                      |--|
103     WLVTIARLRGEHTMQDRLAKEILDAANNTGAAVKKREDTHRMAEANRAFAHFRW
                                                                      153

-------
1 match found in sequence:
 a97903 ; TOIG of: a97903  check: 790  from: 1  to: 156
  (from "ctermpir.pep")
  TOIG of: a97903  check: 790  from: 1  to: 156

 P1;A97903 - 30S ribosomal protein S7 [imported] - Streptococcus pneumoniae
  (strain R6)
 C;Species: Streptococcus pneumoniae
 C;Date: 22-Oct-2001 #sequence_revision 22-Oct-2001 #text_change 02-Nov-2001
 C;Accession: A97903
 R;Hoskins, J.A.; Alborn Jr., W.; Arnold, J.; Blaszczak, L.; Burgett, S.;
  DeHoff, B.S.; Estrem, S.; Fritz, L.; Fu, D.J.; Fuller, W.; Geringer, C.;
  Gilmour, R.; Glass, J.S.; Khoja, H.; Kraft, A.; LaGace, R.; LeBlanc, D.J.; Lee,
  L.N.; Lefkowitz, E.J.; Lu, J.; Matsushima, P.; McAhren, S.; McHenney, M.;
  McLeaster, K.; Mundy, C.; Nicas, T.I.; Norris, F.H.; O'Gara, M.; Peery, R.;
  Robertson, G.T.; Rockey, P.; Sun, P.M.; Winkler, M.E.
 J. Bacteriol. 183, 5709-5717, 2001
 A;Authors: Yang, Y.; Young-Bellido, M.; Zhao, G.; Zook, C.; Baltz, R.H.;
  Jaskunas, S.R.; Rosteck Jr., P.R.; Skatrud, P.L.; Glass, J.I.
 A;Title: Genome of the Bacterium Streptococcus pneumoniae Strain R6.
 A;Reference number: A97872; MUID:21429245; PMID:11544234
 A;Accession: A97903
 A;Status: preliminary
 A;Molecule type: DNA
 A;Residues: 1-156 <KUR>
 A;Cross-references: GB:AE007317; PIDN:AAK99053.1; PID:g15457798; GSPDB:GN00174
 C;Genetics:
 A;Gene: rpsG
 C;Superfamily: Escherichia coli ribosomal protein S7

  A97903  Length: 156  September 17, 2003 13:09  Type: P  Check: 790  ..
 Found using 'cterm' (kam547.key)

...

                                                                      |--|
103     WLVTIARLRGEHTMQDRLAKEILDAANNTGAAVKKREDTHRMAEANRAFAHFRW
                                                                      153

-------
1 match found in sequence:
 d70364 ; TOIG of: d70364  check: 4544  from: 1  to: 160
  (from "ctermpir.pep")
  TOIG of: d70364  check: 4544  from: 1  to: 160

 P1;D70364 - ribosomal protein S07 - Aquifex aeolicus
 C;Species: Aquifex aeolicus
 C;Date: 08-May-1998 #sequence_revision 08-May-1998 #text_change 13-Aug-1999
 C;Accession: D70364
 R;Deckert, G.; Warren, P.V.; Gaasterland, T.; Young, W.G.; Lenox, A.L.; Graham,
  D.E.; Overbeek, R.; Snead, M.A.; Keller, M.; Aujay, M.; Huber, R.; Feldman,
  R.A.; Short, J.M.; Olson, G.J.; Swanson, R.V.
 Nature 392, 353-358, 1998
 A;Title: The complete genome of the hyperthermophilic bacterium Aquifex
  aeolicus.
 A;Reference number: A70300; MUID:98196666; PMID:9537320
 A;Accession: D70364
 A;Status: preliminary; nucleic acid sequence not shown; translation not shown
 A;Molecule type: DNA
 A;Residues: 1-160 <AQF>
 A;Cross-references: GB:AE000705; NID:g2983310; PIDN:AAC06909.1; PID:g2983319;
  GB:AE000657
 A;Experimental source: strain VF5
 C;Genetics:
 A;Gene: rpsG2
 C;Superfamily: Escherichia coli ribosomal protein S7
```

Found using 'cterm' (kam547.key)

...

```
                                                                  |--|
103     WLVTIARLRGEHTMQDRLAKEILDAANNTGAAVKKREDTHRMAEANRAFAHFRW
                                                                  153
```

-- Search Statistics --

Times:	CPU	Total Elapsed
	00:00:00.00	00:00:03.00

Number of sequences searched:	43
Number of sequence hits:	43
Number of separate matches:	43
Number of sequence hits saved:	0

```
        |--|
1       HFRW
        1  4

-------
1 match found in sequence:
 abp81539 ; Streptococcus pneumoniae polypeptide SEQ ID NO 617.
  (from "ctermags.pep")
  TOIG of: abp81539  check: 988  from: 1  to: 156

 ID   ABP81539 standard; Protein; 156 AA.
 XX
 AC   ABP81539;
 XX
 DT   04-MAR-2003  (first entry)
 XX
 DE   Streptococcus pneumoniae polypeptide SEQ ID NO 617.
 XX
 KW   Streptococcus pneumoniae; infection; otitis media; antibacterial;
 KW   diagnosis; gene therapy.
 XX
 OS   Streptococcus pneumoniae.
 XX
 PN   WO200283855-A2.
 XX
 PD   24-OCT-2002.
 XX
 PF   12-APR-2002; 2002WO-US11524.
 XX
 PR   16-APR-2001; 2001US-283948P.
 PR   18-APR-2001; 2001US-284443P.
 XX
 PA   (AMCY ) AMERICAN CYANAMID CO.
 XX
 PI   Zagursky RJ,  Masi AW,  Green BA,  Chakravarti DN,  Russell DP;
 PI   Wooters JL;
 XX
 DR   WPI; 2003-093010/08.
 DR   N-PSDB; ABZ42387.
 XX
 PT   New Streptococcus pneumoniae polynucleotides, useful for treating or
 PT   preventing S. pneumoniae infections, or non-systemic diseases, e.g.
 PT   otitis media, which are induced or exacerbated by S. pneumoniae  -
 XX
 PS   Claim 42; Page 857-858; 1091pp; English.
 XX
 CC   The invention relates to isolated polynucleotides (ABZ72147-ABZ42522) of
 CC   a Streptococcus pneumoniae genomic sequence, a fragment or degenerate
 CC   variant of the polynucleotide or a nucleic acid sequence 95% identical to
 CC   one of the polynucleotides. The S. pneumoniae polynucleotides and
 CC   encoded polypeptides (ABP81299-ABP81674) are useful for treating or
 CC   preventing S. pneumoniae infections or non-systemic diseases, e.g. otitis
 CC   media, which are induced or exacerbated by S. pneumoniae. These are also
 CC   useful for detecting S. pneumoniae in a biological sample or diagnosing
 CC   S. pneumoniae infection in a subject. The polynucleotides have
 CC   antibacterial activity and are useful in gene therapy.
 XX
 SQ   Sequence   156 AA;

 ABP81539  Length: 156  September 17, 2003 13:08  Type: P  Check: 988  ..
 Found using 'cterm' (kam547.key)

...

                                                          |--|
103     WLVTIARLRGEHTMQDRLAKEILDAANNTGAAVKKREDTHRMAEANRAFAHFRW
                                                         153

-------
1 match found in sequence:
 abu00619 ; S. pneumoniae type 4 strain protein from coding region #186.
  (from "ctermags.pep")
  TOIG of: abu00619  check: 988  from: 1  to: 156

 ID   ABU00619 standard; Protein; 156 AA.
 XX
 AC   ABU00619;
 XX
 DT   11-FEB-2003  (first entry)
 XX
 DE   S. pneumoniae type 4 strain protein from coding region #186.
 XX
 KW   Bacterial meningitis; pneumonia; sepsis; otitis media;
 KW   ear infection; antiinflammatory; antibacterial; immunostimulant;
 KW   auditory; respiratory; gene therapy; vaccine.
 XX
 OS   Streptococcus pneumoniae type 4 strain.
 XX
 PN   WO200277021-A2.
 XX
 PD   03-OCT-2002.
 XX
 PF   27-MAR-2002; 2002WO-IB02163.
 XX
 PR   27-MAR-2001; 2001GB-0007658.
 XX
 PA   (CHIR-) CHIRON SPA.
 PA   (GENO-) INST GENOMIC RES.
 XX
 PI   Masignani V,  Tettelin H,  Fraser C;
 XX
 DR   WPI; 2003-040579/03.
 DR   N-PSDB; ABX05898.
 XX
 PT   New proteins and nucleic acid molecules from Streptococcus pneumoniae,
 PT   useful as medicaments for treating or preventing a disease or infection
 PT   due to streptococcus bacteria, such as pneumonia, sepsis, otitis media
 PT   or ear infection  -
 XX
 PS   Claim 1; SEQ ID No 372; 56pp; English.
 XX
 CC   The invention relates to a protein comprising or having at least 50%
 CC   identity to any of the 2469 amino acid sequences, identified in the
 CC   specification (available on a computer readable format), or its fragment,
 CC   expressed from 2469 of 2489 identified DNA coding regions from the
 CC   Streptococcus pneumoniae type 4 strain genomic sequence appearing as
 CC   ABS56454. Also included are an antibody which binds one of the
 CC   proteins, treating a patient by administering the protein, DNA or
 CC   antibody (in a composition), a kit comprising first and second primers,
 CC   which are the nucleic acid cited above or fragments between nucleotides
 CC   8-100 of a sequence not defined in the specification, for amplifying a
 CC   target sequence contained within a Streptococcus nucleic acid sequence,
 CC   where the first primer is substantially complementary to the target
 CC   sequence and the second primer is substantially complementary to the
 CC   complement of the target sequence, and where the parts of the primers
 CC   having substantial complementarity define the termini of the target
 CC   sequence to be amplified, assay comprising contacting a test compound
 CC   with the protein, and determining whether the test compound binds to the
 CC   protein and a Streptococcus  pneumoniae bacterium, where one or more
 CC   genes encoding the proteins has been rendered inactive. The proteins,
 CC   nucleic acid molecules, antibody and compositions are useful as
 CC   medicaments for treating or preventing a disease or infection due to
 CC   streptococcus bacteria, particularly S. pneumoniae, such as pneumonia,
 CC   sepsis, otitis media or ear infection. They are also useful in developing
 CC   vaccines, diagnostics and antibiotics. The methods are useful for
 CC   identifying immunodominant proteins. The present sequence is one of
 CC   the 2469 proteins expressed by the identified coding regions from the
 CC   genomic sequence.
 CC   Note: The sequence data for this patent did not form part
 CC   of the printed specification, but was obtained in electronic
 CC   format directly from WIPO at
 CC   ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ   Sequence   156 AA;

 ABU00619  Length: 156  September 17, 2003 13:08  Type: P  Check: 988  ..
```

ABP29105 Length: 156 September 17, 2003 13:08 Type: P Check: 9938 ..
Found using 'cterm' (kam547.key)

...

```
                                                                |--|
103     WLVNASRARGEHTMKDRLAKEIMDAANNTGASVKKREDTHKMAEANRAFAHFRW
                                                                153
```

---
1 match found in sequence:
abp30760 ; Streptococcus polypeptide SEQ ID NO 10696.
(from "ctermags.pep")
TOIG of: abp30760 check: 9852 from: 1 to: 156

ID ABP30760 standard; Protein; 156 AA.
XX
AC ABP30760;
XX
DT 02-JUL-2002 (first entry)
XX
DE Streptococcus polypeptide SEQ ID NO 10696.
XX
KW Streptococcus; GAS; GBS; group B streptococcus; Streptococcus agalactiae;
KW group A streptococcus; Streptococcus pyogenes; antibacterial;
KW antiinflammatory; infection; vaccine; meningitis; gene therapy.
XX
OS Streptococcus agalactiae.
XX
PN WO200234771-A2.
XX
PD 02-MAY-2002.
XX
PF 29-OCT-2001; 2001WO-GB04789.
XX
PR 27-OCT-2000; 2000GB-0026333.
PR 24-NOV-2000; 2000GB-0028727.
PR 07-MAR-2001; 2001GB-0005640.
XX
PA (CHIR-) CHIRON SPA.
PA (GENO-) INST GENOMIC RES.
XX
PI Telford J, Masignani V, Margarit Ros YI, Grandi G, Fraser C;
PI Tettelin H;
XX
DR WPI; 2002-352536/38.
DR N-PSDB; ABN71391.
XX
PT New Streptococcus protein for the treatment or prevention of infection
PT or disease caused by Streptococcus bacteria, such as meningitis, and
PT for detecting a compound that binds to the protein -
XX
PS Claim 1; Page 4179; 4525pp; English.
XX
CC The invention relates to a protein (ABP25413-ABP30895) from group B
CC streptococcus/GBS (Streptococcus agalactiae) or group A streptococcus/GAS
CC (Streptococcus pyogenes), comprising one of 5483 sequences (S1), given in
CC the specification. The proteins have antibacterial and antiinflammatory
CC activity. (I), nucleic acids encoding (I), ABN66044-ABN71526 and
CC antibodies that bind (I) are used in the manufacture of medicaments for
CC the treatment or prevention of infection or disease caused by
CC Streptococcus bacteria, particularly S. agalactiae and S. pyrogenes.
CC Nucleic acids encoding (I) are used to detect Streptococcus in a
CC biological sample. (I) is used to determine whether a compound binds to
CC (I). A composition comprising (I) or a nucleic acid encoding (I), may be
CC used as a vaccine or diagnostic composition. The disease caused by
CC Streptococcus that is prevented or treated may be meningitis. Nucleic
CC acid encoding (I) may be used to recombinantly produce (I) and may be
CC used in gene therapy. Antibodies to (I) are used for affinity
CC chromatography, immunoassays, and distinguishing/identifying
CC Streptococcus proteins.
XX
SQ Sequence 156 AA;

ABP30760 Length: 156 September 17, 2003 13:08 Type: P Check: 9852 ..
Found using 'cterm' (kam547.key)

...

```
                                                                |--|
103     WLVNASRARGEHTMKDRLAKEIMDAANNTGASVKKREDTHKMAEANRAFAHFRW
                                                                153
```

---
1 match found in sequence:
abp56273 ; Melanocortin peptide active core sequence alpha-MSH SEQ ID NO:1.
(from "ctermags.pep")
TOIG of: abp56273 check: 806 from: 1 to: 4

ID ABP56273 standard; peptide; 4 AA.
XX
AC ABP56273;
XX
DT 11-MAR-2003 (first entry)
XX
DE Melanocortin peptide active core sequence alpha-MSH SEQ ID NO:1.
XX
KW Melanocortin; alpha-melanocyte-stimulating hormone; alpha-MSH;
KW metallopeptide; sexual dysfunction; vasotropic; sexual response.
XX
OS Synthetic.
XX
PN WO200264091-A2.
XX
PD 22-AUG-2002.
XX
PF 13-FEB-2002; 2002WO-US04431.
XX
PR 13-FEB-2001; 2001US-268591P.
XX
PA (PALA-) PALATIN TECHNOLOGIES INC.
XX
PI Sharma SD, Shi Y, Yang W, Cai H, Shadiack A;
XX
DR WPI; 2003-046721/04.
XX
PT Construct useful for eliciting sexual response comprises metal
PT ion-binding domain comprising at least two linked residues -
XX
PS Disclosure; Page 4; 58pp; English.
XX
CC The present invention describes a construct comprising a metal ion-
CC binding domain comprising at least two (preferably 3) linked residues
CC forming an N3S1 ligand available for complexing with a metal ion
CC (preferably rhenium ion). Also described: (1) a manufactured peptide and
CC its salts which comprises the metal ion-binding domain having at least
CC two contiguous amino acids and a determined biological function domain
CC that is an agonist specific for at least one of melanocortin receptors
CC MC-3 or MC-4, and at least a portion of the biological function domain is
CC co-extensive with at least a portion of the metal ion-binding domain and
CC conformationally constrained upon complexing the metal ion binding domain
CC with a metal ion; and (2) a metallopeptide (I) which can be used for the
CC manufacture of a composition for treating sexual dysfunction in a mammal
CC including erectile dysfunction in a male. (I) has vasotropic activity,
CC and can be used for eliciting or stimulating a sexual response and for
CC treating sexual dysfunction e.g. male sexual dysfunction such as erectile
CC dysfunction and female sexual dysfunction. The present sequence
CC represents the melanocortin peptide active core sequence of alpha-
CC melanocyte-stimulating hormone (MSH), which is given in the
CC exemplification of the present invention.
XX
SQ Sequence 4 AA;

ABP56273 Length: 4 September 17, 2003 13:08 Type: P Check: 806 ..
Found using 'cterm' (kam547.key)

```
        |--|
1       EHFRW
        2  5

-------
1 match found in sequence:
 abg94505 ; Alpha-melanocyte-stimulating hormone (alpha-MSH) peptide analogue #
  (from "ctermags.pep")
  TOIG of: abg94505  check: 806  from: 1  to: 4

 ID   ABG94505 standard; Peptide; 4 AA.
 XX
 AC   ABG94505;
 XX
 DT   27-NOV-2002  (first entry)
 XX
 DE   Alpha-melanocyte-stimulating hormone (alpha-MSH) peptide analogue #1.
 XX
 KW   Vasoactive intestinal polypeptide; VIP; female sexual dysfunction;
 KW   vulva; vagina; vaginal atrophy; pain; intercourse; vaginal itching;
 KW   vaginal dryness; sexual desire enhancement; female genitalia; frigidity;
 KW   sexual aversion; menopausal state; post-menopausal state; sexual desire;
 KW   sexual activity; multiple sclerosis; atherosclerosis; diabetes mellitus;
 KW   peripheral neuropathy; autonomic neuropathy; anorgasmia; hypoxia;
 KW   vaginal muscle tone; vaginal lubrication; collagen misdeposition;
 KW   alpha-melanocyte-stimulating hormone; alpha-MSH; melanocortin peptide.
 XX
 OS   Unidentified.
 XX
 PN   US2002099003-A1.
 XX
 PD   25-JUL-2002.
 XX
 PF   13-AUG-2001; 2001US-0929818.
 XX
 PR   27-OCT-1998;   98US-0181316.
 PR   28-OCT-1997;   97US-0959057.
 PR   28-OCT-1997;   97US-0959064.
 PR   04-FEB-2000; 2000US-0498522.
 XX
 PA   (WILS/) WILSON L F.
 PA   (PLAC/) PLACE V A.
 XX
 PI   Wilson LF,  Place VA;
 XX
 DR   WPI; 2002-697729/75.
 XX
 PT   Treating sexual dysfunction in females comprises administering
 PT   vasoactive intestinal polypeptide or against to vagina and/or vulvar
 PT   region -
 XX
 PS   Disclosure; Page 10; 19pp; English.
 XX
 CC   The invention relates to a method for treating sexual dysfunction in
 CC   females comprising administering a formulation comprising a vasoactive
 CC   agent comprising a vasoactive intestinal polypeptide and/or agonist to
 CC   the vagina and/or vulvar region. The method is used for preventing
 CC   vaginal atrophy and pain during intercourse, for treating vaginal itching
 CC   and dryness, for enhancing sexual desire and responsiveness in females
 CC   and for maintaining improvement of the tissue health of the female
 CC   genitalia. The method is also used for treating persistent or recurrent
 CC   deficiency or absence of sexual fantasies and desire for sexual activity,
 CC   frigidity, sexual aversion, menopausal or post-menopausal state, multiple
 CC   sclerosis, atherosclerosis, peripheral neuropathy, autonomic neuropathy,
 CC   diabetes mellitus, substance-induced decreases in sexual desire and
 CC   responsiveness and primary and secondary anorgasmia. The formulation
 CC   improves vaginal muscle tone and tissue health, increases vaginal
 CC   lubrication and minimises collagen misdeposition resulting from hypoxia.
 CC   This sequence represents an alpha-melanocyte-stimulating hormone
 CC   (alpha-MSH) peptide analogue (also referred to as a melanocortin
 CC   peptide), used as a vasoactive agent.
 XX
 SQ   Sequence   4 AA;

  ABG94505  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
 Found using 'cterm' (kam547.key)

        |--|
1       HFRW
        1  4

-------
1 match found in sequence:
 abp29105 ; Streptococcus polypeptide SEQ ID NO 7386.
  (from "ctermags.pep")
  TOIG of: abp29105  check: 9938  from: 1  to: 156

 ID   ABP29105 standard; Protein; 156 AA.
 XX
 AC   ABP29105;
 XX
 DT   02-JUL-2002  (first entry)
 XX
 DE   Streptococcus polypeptide SEQ ID NO 7386.
 XX
 KW   Streptococcus; GAS; GBS; group B streptococcus; Streptococcus agalactiae;
 KW   group A streptococcus; Streptococcus pyogenes; antibacterial;
 KW   antiinflammatory; infection; vaccine; meningitis; gene therapy.
 XX
 OS   Streptococcus pyogenes.
 XX
 PN   WO200234771-A2.
 XX
 PD   02-MAY-2002.
 XX
 PF   29-OCT-2001; 2001WO-GB04789.
 XX
 PR   27-OCT-2000; 2000GB-0026333.
 PR   24-NOV-2000; 2000GB-0028727.
 PR   07-MAR-2001; 2001GB-0005640.
 XX
 PA   (CHIR-) CHIRON SPA.
 PA   (GENO-) INST GENOMIC RES.
 XX
 PI   Telford J,  Masignani V,  Margarit Ros YI,  Grandi G,  Fraser C;
 PI   Tettelin H;
 XX
 DR   WPI; 2002-352536/38.
 DR   N-PSDB; ABN69736.
 XX
 PT   New Streptococcus protein for the treatment or prevention of infection
 PT   or disease caused by Streptococcus bacteria, such as meningitis, and
 PT   for detecting a compound that binds to the protein -
 XX
 PS   Claim 1; Page 3888; 4525pp; English.
 XX
 CC   The invention relates to a protein (ABP25413-ABP30895) from group B
 CC   streptococcus/GBS (Streptococcus agalactiae) or group A streptococcus/GAS
 CC   (Streptococcus pyogenes), comprising one of 5483 sequences (S1), given in
 CC   the specification. The proteins have antibacterial and antiinflammatory
 CC   activity. (I), nucleic acids encoding (I), ABN66044-ABN71526 and
 CC   antibodies that bind (I) are used in the manufacture of medicaments for
 CC   the treatment or prevention of infection or disease caused by
 CC   Streptococcus bacteria, particularly S. agalactiae and S. pyrogenes.
 CC   Nucleic acids encoding (I) are used to detect Streptococcus in a
 CC   biological sample. (I) is used to determine whether a compound binds to
 CC   (I). A composition comprising (I) or a nucleic acid encoding (I), may be
 CC   used as a vaccine or diagnostic composition. The disease caused by
 CC   Streptococcus that is prevented or treated may be meningitis. Nucleic
 CC   acid encoding (I) may be used to recombinantly produce (I) and may be
 CC   used in gene therapy. Antibodies to (I) are used for affinity
 CC   chromatography, immunoassays, and distinguishing/identifying
 CC   Streptococcus proteins.
 XX
 SQ   Sequence   156 AA;
```

```
CC   interact with and inhibit or activate such a polypeptide. The
CC   polypeptides (or DNA encoding them, via gene therapy) are also useful
CC   for inducing an immunological response in a mammal. The antagonists are
CC   useful to inhibit such bacterial polypeptides. The polypeptides are
CC   particularly useful to identify antimicrobial compounds and antibiotics.
CC   They are also useful to determine their role in pathogenesis of
CC   infection, dysfunction and disease.
XX
SQ   Sequence   156 AA;

AAY86085  Length: 156  September 17, 2003 13:08  Type: P  Check: 790  ..
Found using 'cterm' (kam547.key)

...

                                                              |--|
103     WLVTIARLRGEHTMQDRLAKEILDAANNTGAAVKKREDTHRMAEANRAFAHFRW
                                                             153

-------
1 match found in sequence:
abb55616 ; Lactococcus lactis protein rpsG.
 (from "ctermags.pep")
 TOIG of: abb55616  check: 8558  from: 1  to: 155

ID   ABB55616 standard; Protein; 155 AA.
XX
AC   ABB55616;
XX
DT   16-MAY-2002  (first entry)
XX
DE   Lactococcus lactis protein rpsG.
XX
KW   Biosynthesis; biodegradation; lactic bacterium; yogurt; cheese.
XX
OS   Lactococcus lactis IL1403.
XX
PN   FR2807446-A1.
XX
PD   12-OCT-2001.
XX
PF   11-APR-2000; 2000FR-0004630.
XX
PR   11-APR-2000; 2000FR-0004630.
XX
PA   (INRG ) INRA INST NAT RECH AGRONOMIQUE.
XX
PI   Bolotine A,  Sorokine A,  Renault P,  Ehrlich SD;
XX
DR   WPI; 2002-043418/06.
XX
PT   New nucleotide sequence useful in the identification or Lactococcus
PT   lactis and related species -
XX
PS   Claim 6; SEQ ID No 2318; 2504pp; French.
XX
CC   The present invention is related to a Lactococcus lactis nucleotide
CC   sequence (ABA90521) and related proteins (ABB53300-ABB55621). The
CC   nucleic acid sequence is useful in the detection and/or amplification of
CC   nucleic acid sequence, particularly to identify Lactococcus lactis or
CC   related species. The proteins of the invention are useful for the
CC   biosynthesis or biodegradation of a composition of interest. The
CC   invention helps research in lactic bacteria, particularly useful in the
CC   production of yogurt and cheese.
CC   Note: The sequence data for this patent is based on equivalent patent
CC   WO200177334 (published 18-OCT-2001) which is available in electronic
CC   format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   155 AA;

ABB55616  Length: 155  September 17, 2003 13:08  Type: P  Check: 8558  ..
Found using 'cterm' (kam547.key)

...

                                                              |--|
102     WLVTIARNRGEHTMQDRLAKEILDAANNTGAAVKKREDTHKMAEANRAFAHFRW
                                                             152

-------
1 match found in sequence:
abb76167 ; Melanocortin stimulating hormone core peptide.
 (from "ctermags.pep")
 TOIG of: abb76167  check: 1186  from: 1  to: 5

ID   ABB76167 standard; Peptide; 5 AA.
XX
AC   ABB76167;
XX
DT   22-JUL-2002  (first entry)
XX
DE   Melanocortin stimulating hormone core peptide.
XX
KW   Melanocortin stimulating hormone; MSH; human; diabetes; obesity;
KW   insulin resistance; antidiabetic.
XX
OS   Homo sapiens.
XX
PN   WO200223184-A1.
XX
PD   21-MAR-2002.
XX
PF   13-SEP-2001; 2001WO-US28720.
XX
PR   13-SEP-2000; 2000US-232292P.
XX
PA   (ROOS-) ROOSEVELT INST ELEANOR.
PA   (OKLA-) OKLAHOMA MEDICAL RES FOUND.
XX
PI   Brennan MB,  Hochgeschwender U;
XX
DR   WPI; 2002-401913/43.
XX
PT   Identifying compounds useful in regulating insulin resistance in
PT   obesity and type II diabetes by using a proopiomelanocortin null mutant
PT   non-human animal as a model -
XX
PS   Disclosure; Page 19; 70pp; English.
XX
CC   The present sequence is the core peptide sequence of a
CC   melanocortin stimulating hormone (MSH).  It corresponds to amino
CC   acid residues 5-9 of human alpha-MSH (see ABB76168).  A claimed
CC   method of identifying compounds useful in regulating insulin
CC   resistance in obesity and type II diabetes involves administering
CC   a compound having MSH biological activity to a genetically modified
CC   non-human animal that has a genetic modification within 2 alleles
CC   of its Pomc locus that result in an absence of proopiomelanocortin
CC   (Pomc) peptide activity, where administration of the compound
CC   induces insulin resistance in the animal, and selecting compounds
CC   that decrease insulin resistance in the animal.  The compound
CC   having MSH biological activity is MSH or its fragment, homologue,
CC   peptide or non-peptide mimetic, or fusion protein.  The compound to
CC   be evaluated is preferably an MSH antagonist.  A claimed method of
CC   decreasing insulin resistance in a mammal involves administering an
CC   MSH antagonist, especially an MSH fragment, homologue, mimetic or
CC   fusion protein having antagonist action, a soluble MSH receptor,
CC   or an antibody that selectively binds to MSH.  A claimed method to
CC   treat diabetes associated with insulin resistance comprises
CC   administering a composition comprising an MSH antagonist that
CC   decreases insulin resistance.
XX
SQ   Sequence   5 AA;

ABB76167  Length: 5  September 17, 2003 13:08  Type: P  Check: 1186  ..
Found using 'cterm' (kam547.key)
```

PF 22-JUL-1999; 99WO-GB02392.
XX
PR 24-JUL-1998; 98GB-0016234.
XX
PA (HARV-) HARVEY RES LTD WILLIAM.
XX
PI Perretti M, Getting S, Flower R;
XX
DR WPI; 2000-182651/16.
XX
PT Inhibition of neutrophil chemoattractant production, inhibition of
PT polymorphonuclear cell accumulation or reduction/treatment of
PT inflammation using compounds comprising the peptide sequence HFRW -
XX
PS Claim 1; Page 13; 20pp; English.
XX
CC The invention relates to the use of a compound comprising an amino acid
CC sequence His-Phe-Arg-Trp (the present sequence) in the manufacture of a
CC medicament and/or an agonist of melanocortin receptor type 3 (MC3-R)
CC where the compound is not adrenocorticotrophic hormone (ACTH)1-39. The
CC compounds are used to inhibit neutrophil chemoattractant production,
CC polymorphonuclear cell (PMN) accumulation or reduction/treatment of
CC inflammation. Especially, these compounds are agonists of the MC3-R. The
CC inflammatory response/disease is selected from gout, gouty arthritis,
CC rheumatoid arthritis, asthma, reperfusion injury or damage, stroke,
CC myocardial infarction, septic shock, or a skin disorder.
XX
SQ Sequence 4 AA;

AAY77732 Length: 4 September 17, 2003 13:08 Type: P Check: 806 ..
Found using 'cterm' (kam547.key)

|--|
1 HFRW
1 4

---
1 match found in sequence:
aay80507 ; Human melanocyte stimulating hormone peptide consensus sequence #1.
(from "ctermags.pep")
TOIG of: aay80507 check: 806 from: 1 to: 4

ID AAY80507 standard; peptide; 4 AA.
XX
AC AAY80507;
XX
DT 06-JUN-2000 (first entry)
XX
DE Human melanocyte stimulating hormone peptide consensus sequence #1.
XX
KW Vulnerary; dermatological; antiinflammatory; scarring; human; wounds;
KW alpha-melanocyte stimulating hormone; proinflammatory cytokine inhibitor;
KW nitric oxide synthase regulator; antiinflammatory IL-10 synthesis;
KW pulmonary fibrosis; trauma; intestinal obstruction; vision; hearing.
XX
OS Homo sapiens.
XX
PN WO200004873-A1.
XX
PD 03-FEB-2000.
XX
PF 22-JUL-1999; 99WO-GB02388.
XX
PR 22-JUL-1998; 98GB-0015822.
PR 06-AUG-1998; 98GB-0017143.
XX
PA (SMIN) SMITH & NEPHEW PLC.
XX
PI Ferguson MWJ, Chettibi S;
XX
DR WPI; 2000-195076/17.
XX
PT Use of a neuropeptide for prevention and treatment of scars and chronic
PT wounds -
XX
PS Disclosure; Page 39; 44pp; English.
XX
CC The invention relates to the use of a melanocyte stimulating hormone
CC (MSH), analogue or functional fragment in the treatment of scarring.
CC This sequence represents a consensus sequence found in the various
CC isoforms of the human MSH peptides. MSH is an inhibitor of
CC proinflammatory cytokine production, a regulator of nitric oxide
CC synthase and a stimulator of antiinflammatory IL-10 synthesis. MSH,
CC or its analogues, is useful in the preparation of a composition for
CC the treatment of scarring and chronic wounds, and for improving the
CC appearance of existing scars, especially scarring associated with
CC pulmonary fibrosis, muscular and neuronal trauma, intestinal obstruction,
CC impaired vision and hearing (from scarring of corneal or tympanic
CC membrane) are treated using compositions containing the MSH analogues.
XX
SQ Sequence 4 AA;

AAY80507 Length: 4 September 17, 2003 13:08 Type: P Check: 806 ..
Found using 'cterm' (kam547.key)

|--|
1 HFRW
1 4

---
1 match found in sequence:
aay86085 ; S. pneumoniae derived protein #294.
(from "ctermags.pep")
TOIG of: aay86085 check: 790 from: 1 to: 156

ID AAY86085 standard; Protein; 156 AA.
XX
AC AAY86085;
XX
DT 10-APR-2000 (first entry)
XX
DE S. pneumoniae derived protein #294.
XX
KW Treatment; prevention; disease; diagnosis; gene therapy; screening;
KW bacterial; antimicrobial; antibiotic; pathogenesis; infection.
XX
OS Streptococcus pneumoniae.
XX
PN WO9806734-A1.
XX
PD 19-FEB-1998.
XX
PF 15-AUG-1997; 97WO-US14436.
XX
PR 16-AUG-1996; 96US-0024022.
XX
PA (SMIK) SMITHKLINE BEECHAM CORP.
XX
PI Black MT, Hodgson JE, Knowles DJC, Lonetto MA, Nicholas RO;
PI Stodola RK;
XX
DR WPI; 1998-159452/14.
DR N-PSDB; AAZ96405.
XX
PT Streptococcus pneumoniae proteins and related DNA - useful for
PT screening compounds for antibacterial activity
XX
PS Claim 5; Page 562; 640pp; English.
XX
CC This invention describes novel isolated Streptococcus pneumoniae
CC polynucleotides (see AAZ96173-Z96494) and their encoded proteins (see
CC AAY85792-Y86182). The DNA, vectors and host cells described in the
CC method of the invention are useful for the recombinant expression of the
CC polypeptides. The polypeptides are useful for treatment or prevention of
CC disease, or diagnosis of disease related to expression or activity of
CC such a polypeptide. They can also be used to screen for compounds which

```
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "optionally acetylated"
FT   Misc-difference 2
FT                   /note= "D-form residue"
FT   Modified-site   4
FT                   /note= "D-form residue; optionally C-terminally
FT                          amidated or Trp-OH"
XX
PN   WO9964056-A1.
XX
PD   16-DEC-1999.
XX
PF   10-JUN-1999;   99WO-US13221.
XX
PR   10-JUN-1998;   98US-0095874.
XX
PA   (TREG-) TREGA BIOSCIENCES INC.
XX
PI   Basu A,  Girten BE,  Tuttle RR;
XX
DR   WPI; 2000-147076/13.
XX
PT   Alleviating asthma by administration of a cytokine regulatory agent  -
XX
PS   Claim 13; Page 41; 54pp; English.
XX
CC   This sequence represents an example of a cytokine regulatory agent (CRA)
CC   of the invention having the formula: X1-X2-(D)Phe-Arg-(D)Trp-X3, where
CC   X1 = R1R2N-CHR3-CY1Y2-, hydrogen, acetyl or is absent;
CC   X2 = -N(R1)-CHR4-CY1Y2-His-, His, hydrogen or acetyl;
CC   X3 = -N(R1)-CHR6-(CH2)n-CY1Y2-R5 or R5; Y1 and Y2 = hydrogen, or
CC   together form (thio)carbonyl; R1 = hydrogen, acetyl, Et, benzyl,
CC   benzoyl, tert-butoxycarbonyl, benzyloxycarbonyl, -CH2-CO-(polyethylene
CC   glycol) or A; R2 = hydrogen, acetyl, Et or benzyl; R3 = 1-6C linear or
CC   branched alkyl or 3-6C cycloalkyl; R4 = (CH2)mCONH2, (CH2)mCONHR1 or
CC   (CH)2mCONHA; R5 = hydroxy, OR3, amino, mercapto, methylamino,
CC   benzylamino or A; R6 = hydrogen or R3; A = a pyranose; m = 1-3, and
CC   n = 0-3. The CRA are used to reduce the symptoms of asthma by
CC   potentially reducing the production of pro-inflammatory cytokines.
XX
SQ   Sequence   4 AA;

 AAY67189  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

        |--|
1       HFRW
        1  4

-------
1 match found in sequence:
 aay67192 ; Cytokine regulatory agent #6.
  (from "ctermags.pep")
  TOIG of: aay67192  check: 1678  from: 1  to: 6

 ID   AAY67192 standard; peptide; 6 AA.
 XX
 AC   AAY67192;
 XX
 DT   11-APR-2000  (first entry)
 XX
 DE   Cytokine regulatory agent #6.
 XX
 KW   Anti-asthmatic; cytokine regulatory agent; anti-inflammatory.
 XX
 OS   Synthetic.
 XX
 FH   Key             Location/Qualifiers
 FT   Modified-site   1
 FT                   /label= Nle
 FT                   /note= "N-terminally acetylated"
 FT   Misc-difference 4
 FT                   /note= "D-form residue"
 FT   Modified-site   6
 FT                   /note= "D-form residue; C-terminally amidated"
 XX
 PN   WO9964056-A1.
 XX
 PD   16-DEC-1999.
 XX
 PF   10-JUN-1999;   99WO-US13221.
 XX
 PR   10-JUN-1998;   98US-0095874.
 XX
 PA   (TREG-) TREGA BIOSCIENCES INC.
 XX
 PI   Basu A,  Girten BE,  Tuttle RR;
 XX
 DR   WPI; 2000-147076/13.
 XX
 PT   Alleviating asthma by administration of a cytokine regulatory agent  -
 XX
 PS   Claim 14; Page 42; 54pp; English.
 XX
 CC   This sequence represents an example of a cytokine regulatory agent (CRA)
 CC   of the invention having the formula: X1-X2-(D)Phe-Arg-(D)Trp-X3, where
 CC   X1 = R1R2N-CHR3-CY1Y2-, hydrogen, acetyl or is absent;
 CC   X2 = -N(R1)-CHR4-CY1Y2-His-, His, hydrogen or acetyl;
 CC   X3 = -N(R1)-CHR6-(CH2)n-CY1Y2-R5 or R5; Y1 and Y2 = hydrogen, or
 CC   together form (thio)carbonyl; R1 = hydrogen, acetyl, Et, benzyl,
 CC   benzoyl, tert-butoxycarbonyl, benzyloxycarbonyl, -CH2-CO-(polyethylene
 CC   glycol) or A; R2 = hydrogen, acetyl, Et or benzyl; R3 = 1-6C linear or
 CC   branched alkyl or 3-6C cycloalkyl; R4 = (CH2)mCONH2, (CH2)mCONHR1 or
 CC   (CH)2mCONHA; R5 = hydroxy, OR3, amino, mercapto, methylamino,
 CC   benzylamino or A; R6 = hydrogen or R3; A = a pyranose; m = 1-3, and
 CC   n = 0-3. The CRA are used to reduce the symptoms of asthma by
 CC   potentially reducing the production of pro-inflammatory cytokines.
 XX
 SQ   Sequence   6 AA;

 AAY67192  Length: 6  September 17, 2003 13:08  Type: P  Check: 1678  ..
 Found using 'cterm' (kam547.key)

         |--|
1       XQHFRW
          3  6

 -------
 1 match found in sequence:
  aay77732 ; Peptide used in the manufacture of MC3-R agonist.
   (from "ctermags.pep")
   TOIG of: aay77732  check: 806  from: 1  to: 4

  ID   AAY77732 standard; peptide; 4 AA.
  XX
  AC   AAY77732;
  XX
  DT   19-MAY-2000  (first entry)
  XX
  DE   Peptide used in the manufacture of MC3-R agonist.
  XX
  KW   Medicament; agonist; melanocortin receptor type 3; ACTH; PMN; MC3-R;
  KW   adrenocorticotrophic hormone; neutrophil chemoattractant; antigout;
  KW   polymorphonuclear cell; septic shock; skin disorder; antiarthritic;
  KW   melanocortin receptor; anti-inflammatory; antiasmatic; beta-MSH;
  KW   beta-melanocortin-stimulating hormone.
  XX
  OS   Synthetic.
  XX
  PN   WO200005263-A2.
  XX
  PD   03-FEB-2000.
  XX
```

```
FT                   /note= "N-terminal acetyl"
FT   Misc-difference 4
FT                   /note= "D-form residue"
FT   Modified-site   6
FT                   /note= "D-form residue, C-terminal amide"
XX
PN   WO9722356-A1.
XX
PD   26-JUN-1997.
XX
PF   18-DEC-1996;   96WO-US20378.
XX
PR   19-DEC-1995;   95US-0574556.
XX
PA   (HOUG-) HOUGHTEN PHARM INC.
XX
PI   Maniar M,  Mauch S;
XX
DR   WPI; 1997-341431/31.
XX
PT   Complex of ion exchange resin with bio:polymer drug - especially
PT   cytokine regulatory peptide, protecting drug against enzymatic
PT   degradation on oral administration
XX
PS   Disclosure; Page 12; 36pp; English.
XX
CC   This sequence represents a cytokine regulatory agent peptide. The
CC   invention relates to a novel composition which comprises an ion exchange
CC   resin and a therapeutically effective biopolymer in a form for oral
CC   administration. This invention provides a method of protecting a
CC   therapeutically active bioactive polymer from degradation. These
CC   compounds are useful for oral administration of drugs e.g. of a nucleic
CC   acid to the small or large intestine to modulate the expression of
CC   cellular gene products or treatment of colon cancer or especially for
CC   administration of a cytokine regulatory agent (CRA) peptide to control
CC   aberrant cytokine activity, as occurs in pathological conditions such as
CC   immune and inflammatory responses. The release characteristics of the
CC   biopolymer from the compound in the small or large intestine can be
CC   controlled by selection of the ion exchange resin and optional use of
CC   coatings.
XX
SQ   Sequence   6 AA;

AAW45424  Length: 6  September 17, 2003 13:08  Type: P  Check: 1678  ..
Found using 'cterm' (kam547.key)

          |--|
1       XQHFRW
          3  6

-------
1 match found in sequence:
aay50295 ; Neutrophil-activating pancreatic derived peptide 95.
 (from "ctermags.pep")
 TOIG of: aay50295  check: 2189  from: 1  to: 7

ID   AAY50295 standard; Peptide; 7 AA.
XX
AC   AAY50295;
XX
DT   12-JAN-2000  (first entry)
XX
DE   Neutrophil-activating pancreatic derived peptide 95.
XX
KW   Cell activation; pancreas; treatment; cardiovascular disease; trauma;
KW   inflammatory disease; autoimmune diseases; arthritis; diabetes; stroke;
KW   organ rejection; ischemia; Alzheimer's disease; myocardial infarction;
KW   haemorrhagic shock; diabetic retinopathy; venous insufficiency; angina;
KW   trauma; protease inhibitor; hypertension; sepsis.
XX
OS   Unidentified.
XX
PN   WO9946367-A2.
XX
PD   16-SEP-1999.
XX
PF   11-MAR-1999;   99WO-US05247.
XX
PR   11-MAR-1998;   98US-0038894.
XX
PA   (CELL-) CELL ACTIVATION INC.
PA   (REGC ) UNIV CALIFORNIA.
PA   (SCRI ) SCRIPPS RES INST.
XX
PI   Stoughton RB,  Schmid-Schonbein GW,  Hugli TE,  Kistler E;
XX
DR   WPI; 1999-580234/49.
XX
PT   Use of cell activating compositions in developing products for
PT   diagnosis and treatment of e.g. cardiovascular, inflammatory,
PT   autoimmune or Alzheimer's disease, trauma, arthritis, organ rejection,
PT   diabetes, stroke or ischemia -
XX
PS   Example 9; Page 184; 184pp; English.
XX
CC   This invention describes a novel method for the use and preparation of
CC   cell activating compositions which involves preparing a cell activating
CC   composition comprising (a) homogenizing pancreatic tissue in buffer at
CC   about neutral or higher pH to produce a homogenate; (b) removing
CC   particulates from the homogenate; (c) optionally incubating the
CC   resulting homogenate, with particulates removed, with a protease; and
CC   (d) fractionating the homogenate and selecting fractions that exhibit
CC   cell activation activity. The methods can be used for improving
CC   treatment outcome or reducing risk of treatment of e.g. cardiovascular
CC   disease, inflammatory disease, trauma, autoimmune diseases, arthritis,
CC   organ rejection, diabetes and diabetic complications, stroke, ischemia,
CC   Alzheimer's disease, myocardial infarction, haemorrhagic shock, diabetic
CC   retinopathy, diabetes, venous insufficiency, unstable angina or trauma.
CC   They can be used in the veterinary treatment of a non-human subject.
CC   Protease inhibitors can be used to lower cell activation resulting from
CC   these diseases and deficiencies. The detection of an elevated level of
CC   hydrogen peroxide can be used to detect an inflammatory condition. An
CC   elevated level of hydrogen peroxide in plasma or whole blood and in the
CC   presence of superoxide dismutase (SOD) indicates leukocyte up
CC   regulation, e.g. indicative of the onset of an acute cardiovascular
CC   disorders, such as disease onset or ischemic complications. An elevated
CC   level of hydrogen peroxide in plasma or whole blood and a low level in
CC   the presence of SOD is indicative of a chronic or immune compromised
CC   condition e.g. hypertension or sepsis. AAY50201-Y50334 represent peptides
CC   used in the method of the invention.
XX
SQ   Sequence   7 AA;

AAY50295  Length: 7  September 17, 2003 13:08  Type: P  Check: 2189  ..
Found using 'cterm' (kam547.key)

          |--|
1       YMEHFRW
          4  7

-------
1 match found in sequence:
aay67189 ; Cytokine regulatory agent #3.
 (from "ctermags.pep")
 TOIG of: aay67189  check: 806  from: 1  to: 4

ID   AAY67189 standard; peptide; 4 AA.
XX
AC   AAY67189;
XX
DT   11-APR-2000  (first entry)
XX
DE   Cytokine regulatory agent #3.
XX
KW   Anti-asthmatic; cytokine regulatory agent; anti-inflammatory.
XX
```

```
FT   Misc-difference 4
FT                   /note= "D-form residue"
XX
PN   WO9709995-A1.
XX
PD   20-MAR-1997.
XX
PF   12-SEP-1996;   96WO-US14744.
XX
PR   12-SEP-1995;   95US-0527252.
XX
PA   (HOUG-) HOUGHTEN PHARM INC.
XX
PI   Girten BE,  Omholt P,  Tuttle RR;
XX
DR   WPI; 1997-202003/18.
XX
PT   Reducing severity of gastro-intestinal damage - by administration of
PT   cytokine regulatory agent
XX
PS   Claim 22; Page 19; 22pp; English.
XX
CC   AAW30470-W30474 represent cytokine regulatory elements (CRAs) used in
CC   the method of the invention. CRAs were previously known as cytokine
CC   restraining agents. The method of the invention is for reducing the
CC   severity of gastro-intestinal (GI) damage in an individual susceptible
CC   for developing such damage. The method comprises administering to the
CC   individual an effective dose of a CRA of formula
CC   X1-X2-His-(D)Phe-Arg-(D)Trp-X3 (I) or X4-X5-(D)Phe-Arg-(D)Trp-X3' (II),
CC   in which X1= a group of formula R2R1N-CHR3-C(Y1)(Y2)- (i), H or COCH3;
CC   X2= a group of formula -NR1-CHR4-C(Y1)(Y2)- (ii); X3 = R5 or a group of
CC   formula -NR1-CHR6-(CH2)n-C(Y1)(Y2)-R5 (iii); X4 = H, COCH3, or group of
CC   formula R1R2N-CHR4-C(Y1)(Y2)- (iv), or is absent; X5 = His, H or COCH3;
CC   X3' = NH2, OH or a group (iii); Y1, Y2 = H or together form a carbonyl
CC   or thiocarbonyl; R1= H, COCH3, C2H5, CH2Ph, COPh, COOCH2Ph, COO-t-butyl,
CC   CH2CO-(polyethylene glycol) or A; R2 = H or COCH3; R3 = 1-6C linear or
CC   branched alkyl, or 3-6C cyclic alkyl; R4 = (CH2)mCONH2, (CH2)m-CONHR1 or
CC   (CH2)m-CONHA; R5 = OH, OR3, NH2, SH, NHCH3, NHCH2Ph or A; R6 = H or R3;
CC   Ph = C6H5; m = 1-3; n = 0-3; and A = a carbohydrate. The method can be
CC   used to reduce the severity of GI damage induced by a non-steroidal
CC   anti-inflammatory drug (NSAID), e.g. indomethacin. The GI damage treated
CC   with these sequences can also occur as a result of chronic or hereditary
CC   diseases such as ulcerative colitis, or Crohn's disease.
XX
SQ   Sequence   4 AA;

 AAW30473  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

       |--|
1      HFRW
       1  4

-------
1 match found in sequence:
aaw45420 ; Cytokine regulatory agent #1.
 (from "ctermags.pep")
 TOIG of: aaw45420  check: 806  from: 1  to: 4

ID   AAW45420 standard; peptide; 4 AA.
XX
AC   AAW45420;
XX
DT   14-MAY-1998  (first entry)
XX
DE   Cytokine regulatory agent #1.
XX
KW   Cytokine regulatory agent; oral administration; ion exchange resin;
KW   degradation.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "Optional N-terminal acetyl"
FT   Misc-difference 2
FT                   /note= "D-form residue"
FT   Misc-difference 4
FT                   /note= "D-form residue, optional C-terminal amide"
XX
PN   WO9722356-A1.
XX
PD   26-JUN-1997.
XX
PF   18-DEC-1996;   96WO-US20378.
XX
PR   19-DEC-1995;   95US-0574556.
XX
PA   (HOUG-) HOUGHTEN PHARM INC.
XX
PI   Maniar M,  Mauch S;
XX
DR   WPI; 1997-341431/31.
XX
PT   Complex of ion exchange resin with bio:polymer drug - especially
PT   cytokine regulatory peptide, protecting drug against enzymatic
PT   degradation on oral administration
XX
PS   Disclosure; Page 12; 36pp; English.
XX
CC   This sequence represents a cytokine regulatory agent peptide. The
CC   invention relates to a novel composition which comprises an ion exchange
CC   resin and a therapeutically effective biopolymer in a form for oral
CC   administration. This invention provides a method of protecting a
CC   therapeutically active bioactive polymer from degradation. These
CC   compounds are useful for oral administration of drugs e.g. of a nucleic
CC   acid to the small or large intestine to modulate the expression of
CC   cellular gene products or treatment of colon cancer or especially for
CC   administration of a cytokine regulatory agent (CRA) peptide to control
CC   aberrant cytokine activity, as occurs in pathological conditions such as
CC   immune and inflammatory responses. The release characteristics of the
CC   biopolymer from the compound in the small or large intestine can be
CC   controlled by selection of the ion exchange resin and optional use of
CC   coatings.
XX
SQ   Sequence   4 AA;

 AAW45420  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

       |--|
1      HFRW
       1  4

-------
1 match found in sequence:
aaw45424 ; Cytokine regulatory agent #5.
 (from "ctermags.pep")
 TOIG of: aaw45424  check: 1678  from: 1  to: 6

ID   AAW45424 standard; peptide; 6 AA.
XX
AC   AAW45424;
XX
DT   14-MAY-1998  (first entry)
XX
DE   Cytokine regulatory agent #5.
XX
KW   Cytokine regulatory agent; oral administration; ion exchange resin;
KW   degradation.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /label= Nle
```

```
PF   05-MAR-1996;   96WO-US03112.
XX
PR   12-SEP-1995;   95US-0527056.
PR   06-MAR-1995;   95US-0400983.
PR   07-JUN-1995;   95US-0484262.
XX
PA   (HOUG-) HOUGHTEN PHARM INC.
XX
PI   Andablibi A,  Basu A,  Fagan P,  Girten BE,  Houghten RA;
PI   Loullis CC,  Omholt P,  Suto MJ,  Tuttle RR,  Weber PA;
XX
DR   WPI; 1996-425217/42.
XX
PT   Cytokine regulatory agents modified at the amino or carboxy terminus
PT   - for controlling e.g. diabetes, obesity, septic shock, side
PT   effects of cancer therapy
XX
PS   Claim 17; Page 76; 90pp; English.
XX
CC   The sequences given in AAW00266-72 represent cytokine regulatory
CC   peptides which are modified at the amino or carboxy terminus.  These
CC   peptides are used to enhance or restrain cytokine activity and to treat
CC   e.g. disuse deconditioning, IL-10 activity diseases mediated by nitric
CC   oxide and cytokines, adverse drug reactions, obesity, septic shock and
CC   adverse side effects due to cancer chemotherapy or occurring as in
CC   response to organ transplantation, immune, inflammatory and healing
CC   process disorders, pain, cachexia, adult respiratory distress syndrome
CC   (ARDS), autoimmune diseases esp. allergic reactions or anaphylaxis,
CC   arthritis, inflammatory bowel disease, diabetes, glomerulonephritis,
CC   systemic lupus erythematosus, transplant, atherosclerosis and parasitic
CC   mediated immune dysfunctions such as charged disease, esp. organ damage
CC   caused by ischaemia reperfusion or immunosuppressant partic. cyclosporin.
CC    The peptides also act to increase the oxygen consumption of a subject.
XX
SQ   Sequence   4 AA;

 AAW00271  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

       |--|
1      HFRW
       1  4

-------
1 match found in sequence:
 aaw11572 ; Melanotropin hexapeptide deriv. conjugated to an organic acid.
  (from "ctermags.pep")
  TOIG of: aaw11572  check: 1654  from: 1  to: 6

 ID   AAW11572 standard; peptide; 6 AA.
 XX
 AC   AAW11572;
 XX
 DT   25-MAR-2003  (updated)
 DT   20-MAR-1997  (first entry)
 XX
 DE   Melanotropin hexapeptide deriv. conjugated to an organic acid.
 XX
 KW   Melanotropin; alpha-melanocyte stimulating hormone; alpha-MSH;
 KW   dicarboxylic acid; alpha-monounsaturated fatty acid; melanogenesis;
 KW   allergy; inflammation; treatment.
 XX
 OS   Synthetic.
 XX
 FH   Key             Location/Qualifiers
 FT   Misc-difference 1
 FT                   /label= OTHER
 FT                   /note= "OTHER = 5-Me-Norleucine or 2-N-Me-Nle,
 FT                          conjugated to a dicarboxylic acid or to
 FT                          an alpha-monounsaturated fatty acid (see
 FT                          comments section)"
 FT   Modified-site   4
 FT                   /label= OTHER
 FT                   /note= "OTHER = para-fluoro-Phe"
 FT   Modified-site   6
 FT                   /note= "when there is a 5-Me-Nle residue at
 FT                          position 1, Trp at position 6 is opt.
 FT                          amidated"
 XX
 PN   WO9641815-A2.
 XX
 PD   27-DEC-1996.
 XX
 PF   12-JUN-1996;   96WO-FR00890.
 XX
 PR   12-JUN-1995;   95FR-0006909.
 XX
 PA   (EUBI-) INST EURO BIOLOGIE CELLULAIRE.
 XX
 PI   Dussourd Dhinterland L,  Pinel A;
 XX
 DR   WPI; 1997-065421/06.
 XX
 PT   Conjugates of melanotropin peptide(s) with carboxylic acids - useful
 PT   as anti-allergic and anti-inflammatory agents
 XX
 PS   Claim 7; Page 19; 22pp; German.
 XX
 CC   The present sequence represents three specifically claimed examples
 CC   of melanotropin-derived peptides conjugated to either (i) a
 CC   dicarboxylic acid of formula HOOC-R1-COOH, where R1 = opt.
 CC   substituted alkylene of at least 3C (pref. 3-10C) or (ii) an alpha-
 CC   monounsaturated fatty acid of formula R2-CH=CH-COOH, where R2 = alkyl
 CC   group of at least 6C (pref. 6-10C) substituted by NH2, OH or oxo.
 CC   The acids are pref. adipic acid, alpha-aminoadipic acid, sebacic acid,
 CC   trans-10-hydroxy-2-decenoic acid or trans-9-oxo-2-decenoic acid,
 CC   linked via a salt, ester or amide bond to the N-terminus of the peptide.
 CC   The conjugates are useful for treating allergies (esp. of the skin),
 CC   inflammatory reactions and disorders of melanogenesis.
 CC   (Updated on 25-MAR-2003 to correct PI field.)
 XX
 SQ   Sequence   6 AA;

 AAW11572  Length: 6  September 17, 2003 13:08  Type: P  Check: 1654  ..
 Found using 'cterm' (kam547.key)

         |--|
1       XEHFRW
          3  6

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1 match found in sequence:
 aaw30473 ; Cytokine regulatory agent #3.
  (from "ctermags.pep")
  TOIG of: aaw30473  check: 806  from: 1  to: 4

 ID   AAW30473 standard; peptide; 4 AA.
 XX
 AC   AAW30473;
 XX
 DT   06-FEB-1998  (first entry)
 XX
 DE   Cytokine regulatory agent #3.
 XX
 KW   Cytokine regulatory agent; CRA; cytokine restraining agents; GI damage;
 KW   gastro-intestinal damage; non-steroidal anti-inflammatory drug; therapy;
 KW   NSAID; indomethacin; chronic disease; hereditary disease; cyclic;
 KW   Crohn's disease; ulcerative colitis.
 XX
 OS   Synthetic.
 XX
 FH   Key             Location/Qualifiers
 FT   Misc-difference 1. .4
 FT                   /note= "optionally form cyclic peptide"
 FT   Misc-difference 2
 FT                   /note= "D-form residue"
```

```
PR   13-JUN-2000; 2000US-211268P.
PR   30-MAY-2001; 2001US-294531P.
XX
PA   (GLAX ) GLAXO GROUP LTD.
XX
PI   Haizlip JE,  Ignar DM,  Jayawickreme CK,  King HK,  Liacos JA;
PI   Mills K,  Ruan JJ,  Sauls HR,  Shaffer JE;
XX
DR   WPI; 2002-130740/17.
XX
PT   Screening for candidate compounds that modulate the biological activity
PT   of a target, comprises detecting a signal produced by an indicator upon
PT   interaction between the target and a candidate compound  -
XX
PS   Example 8; Page 44; 84pp; English.
XX
CC   The present invention relates to a high throughput method for screening
CC   candidate compounds for an ability to modulate the biological activity
CC   of a target. The method comprises contacting a substrate with candidate
CC   compound samples which interact with the target in the substrate, and
CC   detecting a signal produced by the indicator upon interaction between
CC   the target and the candidate compound. The method allows rapid and high
CC   throughput screening. The present sequence represents a peptide tested
CC   for validation purposes in a bead-based assay in the methods of the
CC   present invention.
XX
SQ   Sequence   6 AA;

AAU75134  Length: 6  September 17, 2003 13:08  Type: P  Check: 1683  ..
Found using 'cterm' (kam547.key)

          |--|
1       SVHFRW
          3  6

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1 match found in sequence:
aaw00268 ; Cytokine regulatory peptide #3.
 (from "ctermags.pep")
 TOIG of: aaw00268  check: 806  from: 1  to: 4

ID   AAW00268 standard; peptide; 4 AA.
XX
AC   AAW00268;
XX
DT   30-APR-1997  (first entry)
XX
DE   Cytokine regulatory peptide #3.
XX
KW   Cytokine regulatory peptide; disuse deconditioning; IL-10;
KW   nitric oxide; adverse drug reaction; obesity; septic shock;
KW   cancer chemotherapy; organ transplant; cachexia; cyclosporin;
KW   adult respiratory distress syndrome; ARDS; autoimmune disease;
KW   allergic reaction; anaphylaxis; arthritis; inflammatory bowel disease;
KW   diabetes; glomerulonephritis; systemic lupus erythematosus;
KW   transplant; atherosclerosis; organ damage; immunosuppressant.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 2
FT                   /note= "D-form residue"
FT   Misc-difference 4
FT                   /note= "D-form residue"
XX
PN   WO9627386-A1.
XX
PD   12-SEP-1996.
XX
PF   05-MAR-1996;   96WO-US03112.
XX
PR   12-SEP-1995;   95US-0527056.
PR   06-MAR-1995;   95US-0400983.
PR   07-JUN-1995;   95US-0484262.
XX
PA   (HOUG-) HOUGHTEN PHARM INC.
XX
PI   Andablibi A,  Basu A,  Fagan P,  Girten BE,  Houghten RA;
PI   Loullis CC,  Omholt P,  Suto MJ,  Tuttle RR,  Weber PA;
XX
DR   WPI; 1996-425217/42.
XX
PT   Cytokine regulatory agents modified at the amino or carboxy terminus
PT   - for controlling e.g. diabetes, obesity, septic shock, side
PT   effects of cancer therapy
XX
PS   Claim 14; Page 76; 90pp; English.
XX
CC   The sequences given in AAW00266-72 represent cytokine regulatory
CC   peptides which are modified at the amino or carboxy terminus.  These
CC   peptides are used to enhance or restrain cytokine activity and to treat
CC   e.g. disuse deconditioning, IL-10 activity diseases mediated by nitric
CC   oxide and cytokines, adverse drug reactions, obesity, septic shock and
CC   adverse side effects due to cancer chemotherapy or occurring as in
CC   response to organ transplantation, immune, inflammatory and healing
CC   process disorders, pain, cachexia, adult respiratory distress syndrome
CC   (ARDS), autoimmune diseases esp. allergic reactions or anaphylaxis,
CC   arthritis, inflammatory bowel disease, diabetes, glomerulonephritis,
CC   systemic lupus erythematosus, transplant, atherosclerosis and parasitic
CC   mediated immune dysfunctions such as charged disease, esp. organ damage
CC   caused by ischaemia reperfusion or immunosuppressant partic. cyclosporin.
CC    The peptides also act to increase the oxygen consumption of a subject.
XX
SQ   Sequence   4 AA;

 AAW00268  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

        |--|
1       HFRW
        1  4

-------
1 match found in sequence:
aaw00271 ; Cytokine regulatory peptide #6.
 (from "ctermags.pep")
 TOIG of: aaw00271  check: 806  from: 1  to: 4

ID   AAW00271 standard; peptide; 4 AA.
XX
AC   AAW00271;
XX
DT   30-APR-1997  (first entry)
XX
DE   Cytokine regulatory peptide #6.
XX
KW   Cytokine regulatory peptide; disuse deconditioning; IL-10;
KW   nitric oxide; adverse drug reaction; obesity; septic shock;
KW   cancer chemotherapy; organ transplant; cachexia; cyclosporin;
KW   adult respiratory distress syndrome; ARDS; autoimmune disease;
KW   allergic reaction; anaphylaxis; arthritis; inflammatory bowel disease;
KW   diabetes; glomerulonephritis; systemic lupus erythematosus; cyclic;
KW   transplant; atherosclerosis; organ damage; immunosuppressant.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 2
FT                   /note= "D-form residue"
FT   Modified-site   4
FT                   /note= "D-form residue"
XX
PN   WO9627386-A1.
XX
PD   12-SEP-1996.
XX
```

```
PF   09-NOV-1994;   94WO-US12897.
XX
PR   12-NOV-1993;   93US-0151534.
XX
PA   (HOUG-) HOUGHTEN PHARM INC.
XX
PI   Girten BE,  Houghten RA,  Loullis CC,  Suto MJ,  Tuttle RR;
XX
DR   WPI; 1995-193901/25.
XX
PT   Cytokine restraining peptides useful for treating inflammation,
PT   cachexia and patho-immunogenic disease - do not cause total
PT   immunosuppression and minimise damage to healthy tissue.
XX
PS   Claims 24, 27; Page 33; 41pp; English.
XX
CC   The patent discloses new cytokine restraining peptides and their amino-
CC   saccharide conjugates. The peptides contain a core sequence of
CC   His-(D)Phe-Arg-(D)Trp, and may be extended by up to 2 amino acids at
CC   the N-terminal and by 1 amino acid at the C-terminal. The N-terminal may
CC   be acetylated and the C-terminal can be in amide form; or the peptide
CC   can be cyclic, with the C-terminal condensing onto the N-terminal.
CC   The peptides can restrain activity due to elevated levels of
CC   interleukins, interferons and tumour necrosis factors and thus control
CC   immune and inflammatory responses. They are useful in the treatment of
CC   inflammation, pain, cachexia, arthritis, inflammatory bowel disease and
CC   systemic lupus erythematosus (SLE).
CC   The present sequence represents specific examples of the new peptides.
XX
SQ   Sequence   4 AA;

 AAR87663  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

       |--|
1      HFRW
       1  4

-------
1 match found in sequence:
aau37639 ; Streptococcus pneumoniae cellular proliferation protein #68.
 (from "ctermags.pep")
 TOIG of: aau37639  check: 790  from: 1  to: 156

ID   AAU37639 standard; Protein; 156 AA.
XX
AC   AAU37639;
XX
DT   14-FEB-2002  (first entry)
XX
DE   Streptococcus pneumoniae cellular proliferation protein #68.
XX
KW   Antisense; prokaryotic cellular proliferation protein;
KW   antibiotic; antibacterial; drug design.
XX
OS   Streptococcus pneumoniae.
XX
PN   WO200170955-A2.
XX
PD   27-SEP-2001.
XX
PF   21-MAR-2001; 2001WO-US09180.
XX
PR   21-MAR-2000; 2000US-191078P.
PR   23-MAY-2000; 2000US-206848P.
PR   26-MAY-2000; 2000US-207727P.
PR   23-OCT-2000; 2000US-242578P.
PR   27-NOV-2000; 2000US-253625P.
PR   22-DEC-2000; 2000US-257931P.
PR   16-FEB-2001; 2001US-269308P.
XX
PA   (ELIT-) ELITRA PHARM INC.
XX
PI   Haselbeck R,  Ohlsen KL,  Zyskind JW,  Wall D,  Trawick JD,  Carr GJ;
PI   Yamamoto RT,  Xu HH;
XX
DR   WPI; 2001-611495/70.
DR   N-PSDB; AAS55498.
XX
PT   New polynucleotides for the identification and development of
PT   antibiotics, comprise sequences of antisense nucleic acids -
XX
PS   Example 3; Seq ID No 13232; 511pp; English.
XX
CC   The invention relates to antisense inhibitors of genes essential to
CC   prokaryotic cellular proliferation, their use in identifying the
CC   genes, their use in the discovery of novel antibiotics, the essential
CC   genes themselves and the encoded proteins. The prokaryotes used are
CC   Escherichia coli, Staphylococcus aureus, Salmonella typhi, Klebsiella
CC   pneumoniae, Pseudomonas aeruginosa and Enterococcus faecalis. The
CC   invention is also useful for the identification of potential new targets
CC   for antibiotic development. The antisense nucleic acids can also be used
CC   to identify proteins used in proliferation, to express these proteins,
CC   and to obtain antibodies capable of binding to the expressed proteins.
CC   The proteins can be used to screen compounds in rational drug discovery
CC   programmes. The antisense nucleic acid sequence is also useful to screen
CC   for homologous nucleic acids which are required for cell proliferation in
CC   a wide variety of organisms. The present sequence represents an
CC   essential prokaryotic cellular proliferation protein.
CC   Note: The sequence data for this patent did not form part
CC   of the printed specification, but was obtained in electronic
CC   format directly from WIPO at
CC   ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   156 AA;

AAU37639  Length: 156  September 17, 2003 13:08  Type: P  Check: 790  ..
Found using 'cterm' (kam547.key)

...

                                                                    |--|
103     WLVTIARLRGEHTMQDRLAKEILDAANNTGAAVKKREDTHRMAEANRAFAHFRW
                                                                   153

-------
1 match found in sequence:
aau75134 ; Peptide 1 tested for validation in bead-based assay.
 (from "ctermags.pep")
 TOIG of: aau75134  check: 1683  from: 1  to: 6

ID   AAU75134 standard; peptide; 6 AA.
XX
AC   AAU75134;
XX
DT   23-APR-2002  (first entry)
XX
DE   Peptide 1 tested for validation in bead-based assay.
XX
KW   High throughput screening method for candidate compound;
KW   modulation of biological activity; bead-based assay.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "N-terminal acetyl"
FT   Misc-difference 3. .4
FT                   /note= "D-form residues"
XX
PN   WO200196597-A2.
XX
PD   20-DEC-2001.
XX
PF   13-JUN-2001; 2001WO-US19033.
XX
```

```
PD   24-JAN-2002.
XX
PF   16-JUL-2001; 2001WO-US22263.
XX
PR   14-JUL-2000; 2000US-218381P.
PR   18-AUG-2000; 2000US-226382P.
PR   06-OCT-2000; 2000US-238380P.
PR   29-DEC-2000; 2000US-258764P.
PR   14-JUN-2001; 2001US-298317P.
XX
PA   (ZYCO-) ZYCOS INC.
XX
PI   Hedley ML,  Urban R,  Aziz N,  Chen H,  Etemad-Moghadam B,  Yin P;
XX
DR   WPI; 2002-195801/25.
XX
PT   Novel nucleic acid encoding fusion protein comprising alpha-melanocyte
PT   stimulating hormone concatamer or its analog, for treating inflammatory
PT   or autoimmune disorders -
XX
PS   Disclosure; Page 13; 89pp; English.
XX
CC   The present invention relates to a nucleic acid comprising a sequence
CC   encoding a fusion polypeptide having an alpha-melanocyte stimulating
CC   hormone (MSH) concatamer. The sequences are useful for treating an
CC   individual suffering from, or at risk of, a disorder of the immune system
CC   e.g. inflammatory disorder or autoimmune disorder, including rheumatoid
CC   arthritis, asthma, sepsis, cirrhosis, dermatitis, psoriasis, contact
CC   hypersensitivity, inflammatory bowel disease, autoimmune encephalitis,
CC   multiple sclerosis, diabetes, lupus, uveitis and coeliac disease. The
CC   present sequence is a peptide described in the exemplification of the
CC   invention.
XX
SQ   Sequence   5 AA;

AA016996  Length: 5  September 17, 2003 13:08  Type: P  Check: 1186  ..
Found using 'cterm' (kam547.key)

        |--|
1       EHFRW
        2  5

-------
1 match found in sequence:
aar87659 ; His-(D)Phe-Arg-(D)Trp core peptide.
 (from "ctermags.pep")
 TOIG of: aar87659  check: 806  from: 1  to: 4

ID   AAR87659 standard; peptide; 4 AA.
XX
AC   AAR87659;
XX
DT   14-FEB-1996  (first entry)
XX
DE   His-(D)Phe-Arg-(D)Trp core peptide.
XX
KW   cytokine; interferon; interleukin; tumour necrosis factor; TNF;
KW   restraining.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 2
FT                   /note= "D-form residue"
FT   Misc-difference 4
FT                   /note= "D-form residue"
XX
PN   WO9513086-A1.
XX
PD   18-MAY-1995.
XX
PF   09-NOV-1994;   94WO-US12897.
XX
PR   12-NOV-1993;   93US-0151534.
XX
PA   (HOUG-) HOUGHTEN PHARM INC.
XX
PI   Girten BE,  Houghten RA,  Loullis CC,  Suto MJ,  Tuttle RR;
XX
DR   WPI; 1995-193901/25.
XX
PT   Cytokine restraining peptides useful for treating inflammation,
PT   cachexia and patho-immunogenic disease - do not cause total
PT   immunosuppression and minimise damage to healthy tissue.
XX
PS   Claim 1; Page 29; 41pp; English.
XX
CC   The patent discloses new cytokine restraining peptides and their amino-
CC   saccharide conjugates. The peptides contain a core sequence of
CC   His-(D)Phe-Arg-(D)Trp, and may be extended by up to 2 amino acids at
CC   the N-terminal and by 1 amino acid at the C-terminal. The N-terminal may
CC   be acetylated and the C-terminal can be in amide form; or the peptide
CC   can be cyclic, with the C-terminal condensing onto the N-terminal.
CC   The peptides can restrain activity due to elevated levels of
CC   interleukins, interferons and tumour necrosis factors and thus control
CC   immune and inflammatory responses. They are useful in the treatment of
CC   inflammation, pain, cachexia, arthritis, inflammatory bowel disease and
CC   systemic lupus erythematosus (SLE).
CC   The present sequence represents the core sequence described above.
XX
SQ   Sequence   4 AA;

 AAR87659  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

        |--|
1       HFRW
        1  4

-------
1 match found in sequence:
aar87663 ; His-(D)Phe-Arg-(D)Trp or cyclo(His-(D)Phe-Arg-(D)Trp).
 (from "ctermags.pep")
 TOIG of: aar87663  check: 806  from: 1  to: 4

ID   AAR87663 standard; peptide; 4 AA.
XX
AC   AAR87663;
XX
DT   15-FEB-1996  (first entry)
XX
DE   His-(D)Phe-Arg-(D)Trp or cyclo(His-(D)Phe-Arg-(D)Trp).
XX
KW   cytokine; interferon; interleukin; tumour necrosis factor; TNF;
KW   restraining; cyclic.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "this site is optionally alpha-N-acetylated;
FT                          alternatively, the C-terminal D-Trp may be
FT                          condensed onto this residue to give a
FT                          cyclic peptide"
FT   Misc-difference 2
FT                   /note= "D-form residue"
FT   Misc-difference 4
FT                   /note= "D-form residue; this residue is optionally
FT                          in amide form, or it may be condensed
FT                          onto the N-terminal His to form a cyclic
FT                          peptide"
XX
PN   WO9513086-A1.
XX
PD   18-MAY-1995.
XX
```

```
ID   AAG71233 standard; Peptide; 4 AA.
XX
AC   AAG71233;
XX
DT   27-JUL-2001  (first entry)
XX
DE   Melanocortin receptor binding peptide #314.
XX
KW   Melanocortin receptor; MC1-R; MC2-R; MC3-R; MC4-R; metallopeptide;
KW   melanoma; energy homeostasis; food intake; anorexia; inflammation;
KW   sexual dysfunction; tanning agent; obesity.
XX
OS   Unidentified.
XX
PN   WO200113112-A1.
XX
PD   22-FEB-2001.
XX
PF   15-JUN-2000; 2000WO-US16396.
XX
PR   12-AUG-1999;   99US-0148994.
XX
PA   (PALA-) PALATIN TECHNOLOGIES INC.
XX
PI   Sharma SD,  Shi Y,  Yang W,  Cai H;
XX
DR   WPI; 2001-218369/22.
XX
PT   Novel construct for therapeutic use, comprising metal ion-binding
PT   domain with residues forming ligand for complexing metal ion, is
PT   conformationally constrained in structure specific for melanocortin
PT   receptors  -
XX
PS   Disclosure; Page 56; 80pp; English.
XX
CC   The present invention describes a construct comprising a metal
CC   ion-binding domain which is conformationally constrained in a structure
CC   specific for a melanocortin receptor when complexed with a metal ion. The
CC   melanocortin receptor may be MC1-R, MC2-R, MC3-R or MC4-R. The constructs
CC   can be used in the diagnosis and treatment of melanoma, as a tanning
CC   agent, to modify energy metabolism and feeding behaviour, including the
CC   treatment of obesity and anorexia, and to treat sexual dysfunction and
CC   inflammation. The present sequence is a melanocortin receptor binding
CC   peptide described in the exemplification of the invention.
XX
SQ   Sequence   4 AA;

 AAG71233  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

       |--|
1      HFRW
       1  4

-------
1 match found in sequence:
 aam48098 ; Alpha melanotropin stimulating hormone peptide 5.
  (from "ctermags.pep")
  TOIG of: aam48098  check: 806  from: 1  to: 4

 ID   AAM48098 standard; peptide; 4 AA.
 XX
 AC   AAM48098;
 XX
 DT   15-MAR-2002  (first entry)
 XX
 DE   Alpha melanotropin stimulating hormone peptide 5.
 XX
 KW   Alpha melanotropin stimulating hormone; alpha-MSH; cytostatic;
 KW   radioimaging; malignant melanoma; human.
 XX
 OS   Synthetic.
 XX
 FH   Key             Location/Qualifiers
 FT   Misc-difference 2
 FT                   /note= "D-form residue"
 XX
 PN   US2001038822-A1.
 XX
 PD   08-NOV-2001.
 XX
 PF   24-APR-2001; 2001US-0841407.
 XX
 PR   30-APR-1998;   98US-0070276.
 XX
 PA   (JURI/) JURISSON S S.
 PA   (QUIN/) QUINN T P.
 PA   (GIBL/) GIBLIN M F.
 XX
 PI   Jurisson SS,  Quinn TP,  Giblin MF;
 XX
 DR   WPI; 2002-121328/16.
 XX
 PT   Radiopharmaceutical compound useful for diagnosis and treatment of
 PT   cancer contains alpha-melanotropin stimulating hormone  -
 XX
 PS   Example; Page 5; 13pp; English.
 XX
 CC   The invention relates to a pharmaceutical compound containing an
 CC   alpha-melanotropin stimulating hormone analog (alpha-MSH) which has
 CC   integrally located a radionucleotide with cytostatic activity. The
 CC   compound is useful as a diagnostic or therapeutic pharmaceutical for
 CC   radioimaging and for localised radiation of the malignant melanoma in
 CC   warm blooded animal e.g. mammal. The compound displays exceptional
 CC   stability, biodistribution and tumour targeting properties to eliminate
 CC   all cancer cells and their symptoms and achieve more rapid recovery. The
 CC   radiolabeling of the peptide without the use of a separate chelating
 CC   ligand and the peptide linkage group is possible. The present sequence is
 CC   that of a alpha-MSH peptide, useful to the invention.
 XX
 SQ   Sequence   4 AA;

  AAM48098  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
 Found using 'cterm' (kam547.key)

       |--|
1      HFRW
       1  4

-------
1 match found in sequence:
 aao16996 ; Alpha-MSH peptide fragment SEQ ID NO: 41.
  (from "ctermags.pep")
  TOIG of: aao16996  check: 1186  from: 1  to: 5

 ID   AAO16996 standard; Peptide; 5 AA.
 XX
 AC   AAO16996;
 XX
 DT   29-MAY-2002  (first entry)
 XX
 DE   Alpha-MSH peptide fragment SEQ ID NO: 41.
 XX
 KW   Alpha-MSH; inflammation; autoimmune disease; gene therapy; sepsis;
 KW   alpha-melanocyte stimulating hormone; rheumatoid arthritis; asthma;
 KW   cirrhosis; dermatitis; psoriasis; inflammatory bowel disease;
 KW   immunosuppressive; antiinflammatory; antirheumatic; antiarthritic;
 KW   antiasthmatic; antibacterial; dermatological; antipsoriatic;
 KW   antidiabetic; ophthalmological; neuroprotective; multiple sclerosis;
 KW   diabetes; uveitis; coeliac disease.
 XX
 OS   Unidentified.
 XX
 PN   WO200206316-A2.
 XX
```

```
KW   therapy.
XX
OS   Unidentified.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /label= Nle
FT                   /note= "N-terminal acetylated"
FT   Misc-difference 5
FT                   /note= "D-form residue"
FT   Modified-site   7
FT                   /note= "C-terminal amide"
XX
PN   WO200264734-A2.
XX
PD   22-AUG-2002.
XX
PF   19-DEC-2001; 2001WO-US50075.
XX
PR   19-DEC-2000; 2000US-256842P.
PR   11-JUL-2001; 2001US-304835P.
PR   04-OCT-2001; 2001US-327835P.
XX
PA   (PALA-) PALATIN TECHNOLOGIES INC.
XX
PI   Sharma SD,  Shi Y;
XX
DR   WPI; 2002-740699/80.
XX
PT   Determining secondary structure binding to desired targets within
PT   parent polypeptides that bind to targets, by constructing and
PT   complexing peptides to metal ions to form metallopeptides and screening
PT   the metallopeptides  -
XX
PS   Claim 193; Page 98; 165pp; English.
XX
CC   The invention relates to a method for identification and determination
CC   of target-specific folding sites in peptides and proteins. The invention
CC   also relates to a method for determining a secondary structure binding
CC   to desired targets within parent polypeptides that bind to targets, by
CC   constructing and complexing peptides to metal ions to form
CC   metallopeptides and screening the metallopeptides. The method is useful
CC   for determining secondary structure binding to desired target within
CC   parent polypeptide with primary structure that binds to the target,
CC   where the target of interest is a receptor, antibody, toxin, enzyme,
CC   hormone, nucleic acid, intracellular protein domain of biological
CC   relevance or extracellular protein domain of biological relevance. A
CC   library of amyloid beta-protein related peptides is useful for the
CC   treatment of Alzheimer's disease (AD). A library of peptides targetting
CC   vasopressin, oxytocin or angiotensin receptor is useful for treating
CC   Prion's disease. The present sequence is a peptide used to illustrate
CC   the method of the invention.
XX
SQ   Sequence   7 AA;

AAE29664  Length: 7  September 17, 2003 13:08  Type: P  Check: 2158  ..
Found using 'cterm' (kam547.key)

          |--|
1       XACHFRW
          4  7

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1 match found in sequence:
aae29690 ; Metallopeptide #1 specific for melanocortin receptor 1 (MCR1).
 (from "ctermags.pep")
 TOIG of: aae29690  check: 2158  from: 1  to: 7

ID   AAE29690 standard; peptide; 7 AA.
XX
AC   AAE29690;
XX
DT   27-JAN-2003  (first entry)
XX
DE   Metallopeptide #1 specific for melanocortin receptor 1 (MCR1).
XX
KW   Metallopeptide; nootropic; amyloid beta-protein; Alzheimer's disease; AD;
KW   Prion's disease; oxytocin; angiotensin; vasopressin; neuroprotective;
KW   therapy; melanocortin receptor 1; MCR1.
XX
OS   Unidentified.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /label= Nle
FT                   /note= "N-terminal acetyl"
FT   Misc-difference 5
FT                   /note= "D-form residue"
FT   Modified-site   7
FT                   /note= "C-terminal amide"
XX
PN   WO200264734-A2.
XX
PD   22-AUG-2002.
XX
PF   19-DEC-2001; 2001WO-US50075.
XX
PR   19-DEC-2000; 2000US-256842P.
PR   11-JUL-2001; 2001US-304835P.
PR   04-OCT-2001; 2001US-327835P.
XX
PA   (PALA-) PALATIN TECHNOLOGIES INC.
XX
PI   Sharma SD,  Shi Y;
XX
DR   WPI; 2002-740699/80.
XX
PT   Determining secondary structure binding to desired targets within
PT   parent polypeptides that bind to targets, by constructing and
PT   complexing peptides to metal ions to form metallopeptides and screening
PT   the metallopeptides  -
XX
PS   Example 2; Page 48; 165pp; English.
XX
CC   The invention relates to a method for identification and determination
CC   of target-specific folding sites in peptides and proteins. The invention
CC   also relates to a method for determining a secondary structure binding
CC   to desired targets within parent polypeptides that bind to targets, by
CC   constructing and complexing peptides to metal ions to form
CC   metallopeptides and screening the metallopeptides. The method is useful
CC   for determining secondary structure binding to desired target within
CC   parent polypeptide with primary structure that binds to the target,
CC   where the target of interest is a receptor, antibody, toxin, enzyme,
CC   hormone, nucleic acid, intracellular protein domain of biological
CC   relevance or extracellular protein domain of biological relevance. A
CC   library of amyloid beta-protein related peptides is useful for the
CC   treatment of Alzheimer's disease (AD). A library of peptides targetting
CC   vasopressin, oxytocin or angiotensin receptor is useful for treating
CC   Prion's disease. The present sequence is a metallopeptide specific for
CC   melanocortin receptor 1 (MCR1). This sequence is used to illustrate
CC   the method of the invention.
XX
SQ   Sequence   7 AA;

AAE29690  Length: 7  September 17, 2003 13:08  Type: P  Check: 2158  ..
Found using 'cterm' (kam547.key)

          |--|
1       XACHFRW
          4  7

-------
1 match found in sequence:
aag71233 ; Melanocortin receptor binding peptide #314.
 (from "ctermags.pep")
 TOIG of: aag71233  check: 806  from: 1  to: 4
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XX
PN   WO200206529-A2.
XX
PD   24-JAN-2002.
XX
PF   13-JUL-2001; 2001WO-US22035.
XX
PR   13-JUL-2000; 2000US-218261P.
PR   13-APR-2001; 2001US-283691P.
XX
PA   (UYJO ) UNIV JOHNS HOPKINS SCHOOL MEDICINE.
XX
PI   Germino GG,  Watnick TJ,  Phakdeekitcharoen B;
XX
DR   WPI; 2002-179805/23.
XX
PT   Novel primer for diagnosing polycystic kidney disease-associated
PT   disorder, comprises regions having sequence that selectively hybridizes
PT   to polycystic kidney disease gene sequence  -
XX
PS   Example 2; Page -; 192pp; English.
XX
CC   The present invention relates to compositions and methods useful for the
CC   identification and detection of polycystic kidney disease (PKD1) gene
CC   mutations. The invention also relates to primers comprising a 5' region
CC   having a sequence that selectively hybridises to a PKD1 gene sequence
CC   and optionally, to a PKD1 homologue sequence and an adjacent 3' region
CC   having a sequence that selectively hybridises to a PKD1 gene sequence
CC   and not to a PKD1 homologue sequence. Primer pairs of the invention are
CC   useful for detecting the presence or absence of a mutation in a PKD1
CC   polynucleotide in a sample, for identifying a subject at risk for a
CC   PKD1-associated disorder such as autosomal dominant polycystic kidney
CC   disease (ADPKD) or acquired cystic disease and for diagnosing a PKD1-
CC   associated disorder in a subject. They are useful for selectively
CC   amplifying a region of a PKD1 gene. PKD1 DNA fragments are useful
CC   detecting the presence of a mutant PKD1 polynucleotide in a sample,
CC   as a probe for an amplification reaction, in hybridisation or
CC   amplification assays of biological samples to detect abnormalities
CC   of PKD1 expression and for engineering transgenic animals. The present
CC   sequence is human PKD1 truncated protein mutant.
CC   Note: This sequence is not shown in the specification but is derived
CC   from human PKD1 wild type protein shown in pages 156-170 of the
CC   specification.
XX
SQ   Sequence   3001 AA;

AAE18944  Length: 3001  September 17, 2003 13:08  Type: P  Check: 8520  ..
Found using 'cterm' (kam547.key)

...

                                                                  |--|
2948    SEPRPNEHNCSASRRIRPESLQGADHRPYTFFISPGSRDPAGSYHLNLSSHFRW
                                                                2998

-------
1 match found in sequence:
aae29663 ; Melanocortin receptor metallopeptide.
  (from "ctermags.pep")
  TOIG of: aae29663  check: 1646  from: 1  to: 6

ID   AAE29663 standard; peptide; 6 AA.
XX
AC   AAE29663;
XX
DT   27-JAN-2003  (first entry)
XX
DE   Melanocortin receptor metallopeptide.
XX
KW   Metallopeptide; nootropic; amyloid beta-protein; Alzheimer's disease; AD;
KW   Prion's disease; oxytocin; angiotensin; vasopressin; neuroprotective;
KW   melanocortin; therapy.
XX
OS   Unidentified.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /label= Nle
FT   Misc-difference 4
FT                   /note= "D-form residue"
XX
PN   WO200264734-A2.
XX
PD   22-AUG-2002.
XX
PF   19-DEC-2001; 2001WO-US50075.
XX
PR   19-DEC-2000; 2000US-256842P.
PR   11-JUL-2001; 2001US-304835P.
PR   04-OCT-2001; 2001US-327835P.
XX
PA   (PALA-) PALATIN TECHNOLOGIES INC.
XX
PI   Sharma SD,  Shi Y;
XX
DR   WPI; 2002-740699/80.
XX
PT   Determining secondary structure binding to desired targets within
PT   parent polypeptides that bind to targets, by constructing and
PT   complexing peptides to metal ions to form metallopeptides and screening
PT   the metallopeptides  -
XX
PS   Claim 192; Page 97; 165pp; English.
XX
CC   The invention relates to a method for identification and determination
CC   of target-specific folding sites in peptides and proteins. The invention
CC   also relates to a method for determining a secondary structure binding
CC   to desired targets within parent polypeptides that bind to targets, by
CC   constructing and complexing peptides to metal ions to form
CC   metallopeptides and screening the metallopeptides. The method is useful
CC   for determining secondary structure binding to desired target within
CC   parent polypeptide with primary structure that binds to the target,
CC   where the target of interest is a receptor, antibody, toxin, enzyme,
CC   hormone, nucleic acid, intracellular protein domain of biological
CC   relevance or extracellular protein domain of biological relevance. A
CC   library of amyloid beta-protein related peptides is useful for the
CC   treatment of Alzheimer's disease (AD). A library of peptides targetting
CC   vasopressin, oxytocin or angiotensin receptor is useful for treating
CC   Prion's disease. The present sequence is a melanocortin receptor
CC   metallopeptide used to illustrate the method of the invention.
XX
SQ   Sequence   6 AA;

AAE29663  Length: 6  September 17, 2003 13:08  Type: P  Check: 1646  ..
Found using 'cterm' (kam547.key)

         |--|
1       XAHFRW
          3  6

-------
1 match found in sequence:
aae29664 ; Peptide #2 used to illustrate the method of the invention.
  (from "ctermags.pep")
  TOIG of: aae29664  check: 2158  from: 1  to: 7

ID   AAE29664 standard; peptide; 7 AA.
XX
AC   AAE29664;
XX
DT   27-JAN-2003  (first entry)
XX
DE   Peptide #2 used to illustrate the method of the invention.
XX
KW   Metallopeptide; nootropic; amyloid beta-protein; Alzheimer's disease; AD;
KW   Prion's disease; oxytocin; angiotensin; vasopressin; neuroprotective;
```

```
XX
CC   The present invention describes a compound for use in the diagnosis and
CC   treatment of cancer, particularly melanoma, where the compound comprises
CC   an alpha-melanotropin stimulating hormone (alpha-MSH) analogue with a
CC   radionuclide integrated into the peptide.
XX
SQ   Sequence   4 AA;

 AAB66335  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

       |--|
1      HFRW
       1  4

-------
1 match found in sequence:
aab67268 ; Sexual dysfunction peptide #2.
 (from "ctermags.pep")
 TOIG of: aab67268  check: 806  from: 1  to: 4

ID   AAB67268 standard; peptide; 4 AA.
XX
AC   AAB67268;
XX
DT   20-APR-2001  (first entry)
XX
DE   Sexual dysfunction peptide #2.
XX
KW   Sexual dysfuction; erectile; penis; sexual arousal disorder;
KW   inflammation.
XX
OS   Synthetic.
XX
PN   WO200105401-A1.
XX
PD   25-JAN-2001.
XX
PF   13-JUL-2000; 2000WO-US19408.
XX
PR   16-JUL-1999;   99US-0356386.
PR   30-JUL-1999;   99US-0364825.
PR   21-SEP-1999;   99US-0401004.
XX
PA   (TREG-) TREGA BIOSCIENCES INC.
XX
PI   Dines KC,  Gahman TC,  Girten BE,  Hitchin DL,  Holme KR,  Lang H;
PI   Slivka SR,  Watson-Straughan KJ,  Tuttle RR,  Pei Y;
XX
DR   WPI; 2001-159469/16.
XX
PT   Treating sexual dysfunction, e.g. erectile dysfunction in male and
PT   sexual arousal disorder in female, comprises administering peptide
PT   compounds which are melanocortin receptor-3 ligands -
XX
PS   Claim 14; Page 7; 59pp; English.
XX
CC   The present invention relates to treating sexual dysfunction in a
CC   subject by administering peptide compounds.
CC   Especially for treating erectile dysfunction in male and sexual
CC   arousal disorder in female. Also for treating inflammation.
XX
SQ   Sequence   4 AA;

 AAB67268  Length: 4  September 17, 2003 13:08  Type: P  Check: 806  ..
Found using 'cterm' (kam547.key)

       |--|
1      HFRW
       1  4

-------
1 match found in sequence:
aab67273 ; Sexual dysfunction peptide #7.
 (from "ctermags.pep")
 TOIG of: aab67273  check: 1678  from: 1  to: 6

ID   AAB67273 standard; peptide; 6 AA.
XX
AC   AAB67273;
XX
DT   20-APR-2001  (first entry)
XX
DE   Sexual dysfunction peptide #7.
XX
KW   Sexual dysfuction; erectile; penis; sexual arousal disorder;
KW   inflammation.
XX
OS   Synthetic.
XX
PN   WO200105401-A1.
XX
PD   25-JAN-2001.
XX
PF   13-JUL-2000; 2000WO-US19408.
XX
PR   16-JUL-1999;   99US-0356386.
PR   30-JUL-1999;   99US-0364825.
PR   21-SEP-1999;   99US-0401004.
XX
PA   (TREG-) TREGA BIOSCIENCES INC.
XX
PI   Dines KC,  Gahman TC,  Girten BE,  Hitchin DL,  Holme KR,  Lang H;
PI   Slivka SR,  Watson-Straughan KJ,  Tuttle RR,  Pei Y;
XX
DR   WPI; 2001-159469/16.
XX
PT   Treating sexual dysfunction, e.g. erectile dysfunction in male and
PT   sexual arousal disorder in female, comprises administering peptide
PT   compounds which are melanocortin receptor-3 ligands -
XX
PS   Claim 16; Page 8; 59pp; English.
XX
CC   The present invention relates to treating sexual dysfunction in a
CC   subject by administering peptide compounds.
CC   Especially for treating erectile dysfunction in male and sexual
CC   arousal disorder in female. Also for treating inflammation.
XX
SQ   Sequence   6 AA;

AAB67273  Length: 6  September 17, 2003 13:08  Type: P  Check: 1678  ..
Found using 'cterm' (kam547.key)

         |--|
1       XQHFRW
          3  6

-------
1 match found in sequence:
aae18944 ; Human PKD1 truncated protein mutant #1.
 (from "ctermags.pep")
 TOIG of: aae18944  check: 8520  from: 1  to: 3001

ID   AAE18944 standard; Protein; 3001 AA.
XX
AC   AAE18944;
XX
DT   17-MAY-2002  (first entry)
XX
DE   Human PKD1 truncated protein mutant #1.
XX
KW   Human; PKD1 gene; autosomal dominant polycystic kidney disease; ADPKD;
KW   acquired cystic disease; transgenic animal; mutant; mutein.
XX
OS   Homo sapiens.
OS   Synthetic.
```

DT 12-FEB-2001 (first entry)
XX
DE Melanocortin receptor ligand cyclic peptide analogue #2.
XX
KW Melanocortin receptor ligand; peptide analogue; cyclic; MC-4; MC-3;
KW obesity; body weight disorder; behaviour; memory; muscle atrophy;
KW cardiovascular function; inflammation; sepsis; sexual dysfunction;
KW nerve growth; foetal growth; CNS depression.
XX
OS Synthetic.
XX
PN WO200058361-A1.
XX
PD 05-OCT-2000.
XX
PF 21-MAR-2000; 2000WO-US07473.
XX
PR 29-MAR-1999; 99US-0126673.
XX
PA (PROC) PROCTER & GAMBLE CO.
XX
PI Mazur AW, Wang F, Sheldon RJ, Ebetino FH;
XX
DR WPI; 2000-664909/64.
XX
PT New cyclopeptide analogs, useful as appetite modulators, are selective
PT MC-3 and MC-4 melanocortin receptor ligands -
XX
PS Disclosure; Page 12; 66pp; English.
XX
CC The present invention relates to a number of cyclic peptide analogues
CC which function as melanocortin receptor ligands. The sequences are given
CC in AAB29201-B29246. These are useful in the treatment of body weight
CC disorders including obesity, anorexia and cachexia, CNS depression,
CC behaviour and memory-related disorders, cardiovascular function,
CC inflammation, sepsis, septic, cardiogenic and hypovolemic shock, sexual
CC dysfunction, erectile dysfunction, muscle atrophy, diseases associated
CC with nerve growth and repair and intrauterine foetal growth.
XX
SQ Sequence 4 AA;

AAB29202 Length: 4 September 17, 2003 13:08 Type: P Check: 806 ..
Found using 'cterm' (kam547.key)

|--|
1 HFRW
1 4

---
1 match found in sequence:
aab61544 ; alpha-melanocyte-stimulating hormone peptide fragment.
(from "ctermags.pep")
TOIG of: aab61544 check: 806 from: 1 to: 4

ID AAB61544 standard; peptide; 4 AA.
XX
AC AAB61544;
XX
DT 03-APR-2001 (first entry)
XX
DE alpha-melanocyte-stimulating hormone peptide fragment.
XX
KW Alpha-melanocyte-stimulating hormone; alpha-MSH; vasotropic;
KW sexual response stimulator; sexual dysfunction; erectile dysfunction.
XX
OS Unidentified.
XX
PN WO200100224-A1.
XX
PD 04-JAN-2001.
XX
PF 29-JUN-2000; 2000WO-US18217.
XX
PR 29-JUN-1999; 99US-0142346.
PR 05-APR-2000; 2000US-0194987.
PR 28-JUN-2000; 2000US-0606501.
XX
PA (PALA-) PALATIN TECHNOLOGIES INC.
XX
PI Blood CH, Shadiack AM, Bernstein JK, Herbert GW;
XX
DR WPI; 2001-137878/14.
XX
PT Novel melanocortin receptor-specific peptides useful for treating
PT sexual dysfunction in mammals, including male sexual dysfunction such
PT as erectile dysfunction, and female sexual dysfunction -
XX
PS Claim 8; Page 23; 33pp; English.
XX
CC The present sequence is a peptide fragment of
CC alpha-melanocyte-stimulating hormone (alpha-MSH). alpha-MSH is a
CC melanocortin receptor-specific peptide. This peptide can be used to
CC produce a pharmaceutical composition, which can be used to stimulate
CC sexual response in a mammal, to treat sexual dysfunction in mammal
CC including male sexual dysfunction such as erectile dysfunction, and
CC female sexual dysfunction. The present sequence is the minimum peptide
CC fragment of native alpha-MSH needed for erectile response.
XX
SQ Sequence 4 AA;

AAB61544 Length: 4 September 17, 2003 13:08 Type: P Check: 806 ..
Found using 'cterm' (kam547.key)

|--|
1 HFRW
1 4

---
1 match found in sequence:
aab66335 ; Alpha melanotropin stimulating hormone core sequence.
(from "ctermags.pep")
TOIG of: aab66335 check: 806 from: 1 to: 4

ID AAB66335 standard; peptide; 4 AA.
XX
AC AAB66335;
XX
DT 05-APR-2001 (first entry)
XX
DE Alpha melanotropin stimulating hormone core sequence.
XX
KW Alpha melanotropin stimulating hormone; alpha-MSH; skin pigmentation;
KW cancer; melanoma; analogue; radiolabel.
XX
OS Unidentified.
XX
PN WO200102022-A1.
XX
PD 11-JAN-2001.
XX
PF 01-MAY-2000; 2000WO-US11672.
XX
PR 19-MAY-1999; 99US-0314444.
XX
PA (UMOR) UNIV MISSOURI.
XX
PI Jurisson SS, Quinn TP, Giblin MF;
XX
DR WPI; 2001-123068/13.
XX
PT Melanotropin analog used as diagnosis or therapeutic pharmaceutical for
PT radioimaging malignant melanoma and subjecting to localized radiation
PT comprises a radionuclide integral in alpha-melanotropin stimulating
PT hormone -
XX
PS Disclosure; Page 2; 43pp; English.

PD 15-JUN-2000.
XX
PF 09-DEC-1999; 99WO-US29337.
XX
PR 09-DEC-1998; 98US-0111581.
PR 29-JUL-1999; 99US-0146299.
PR 29-JUL-1999; 99US-0146300.
PR 29-JUL-1999; 99US-0146301.
PR 29-JUL-1999; 99US-0146302.
PR 29-JUL-1999; 99US-0146303.
PR 29-JUL-1999; 99US-0146304.
PR 29-JUL-1999; 99US-0146305.
PR 29-JUL-1999; 99US-0146306.
PR 12-AUG-1999; 99US-0374827.
XX
PA (ROOS-) ROOSEVELT INST ELEANOR.
PA (OKLA-) OKLAHOMA MEDICAL RES FOUND.
XX
PI Brennan MB, Hochgeschwender U;
XX
DR WPI; 2000-423155/36.
XX
PT Regulating metabolism with pro-opiomelanocortin compounds, useful e.g.
PT for treating obesity, administered peripherally to minimize effects on
PT the central nervous system -
XX
PS Claim 32j; Page -; 168pp; English.
XX
CC The invention relates to methods and compositions for the regulation of
CC body weight, and for the treatment of associated disorders, comprising
CC the administration of a proopiomelanocortin (POMC) compound to
CC peripheral tissues such that delivery to the central nervous system is
CC minimised. The amount of POMC compound used is insufficient to alter
CC appetite and is preferably in the range 0.1 microgram-10 mg/kg. The
CC primary aim of the invention is therefore to effect weight regulation via
CC the control of the lipid mobilisation and sequestration in adipose tissue
CC (peripheral pathways of energy homeostasis) rather than via appetite
CC modification (central pathways of energy homeostasis). The POMC compounds
CC of the invention regulate fat stores in adipose tissue by altering free
CC fatty acid uptake and/or lipolysis. The compounds can be used to treat
CC or prevent disorders of body weight such as obesity, anorexia, bulimia,
CC cachexia and wasting disorders. They can be used to treat disorders that
CC can be associated with obesity (such as cardiovascular disease, certain
CC cancers, type II diabetes and atypical depression), and disorders that
CC can be associated with low body weight (such as heart failure, immune
CC system weakness, amenorrhoea and depression). They can also be used to
CC treat reproductive disorders and the undesirable body weight changes
CC that can be side effects of certain pharmaceuticals. The compounds of
CC the invention include melanocyte stimulatory hormone (MSH) analogues.
CC MSH agonists reduce body weight, while MSH antagonists increase body
CC weight. The invention provides alpha-MSH peptide analogues
CC (AAB11841-B11886) and also discloses a Pomc knockout mouse for the study
CC of peripheral and central energy homeostasis pathways. The present
CC sequence represents an alpha-MSH analogue of the invention.
CC Note: This sequence is not given in full in the specification, but
CC is derived from the native human alpha-MSH given on page 41 (AAB11840)
CC and the information provided on page 137 (claim 32j).
XX
SQ Sequence 6 AA;

AAB11862 Length: 6 September 17, 2003 13:08 Type: P Check: 1654 ..
Found using 'cterm' (kam547.key)

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        |--|
1       XEHFRW
          3  6
```

---
1 match found in sequence:
aab12705 ; Tetrapeptide messase sequence of alpha-MSH.
(from "ctermags.pep")
TOIG of: aab12705 check: 806 from: 1 to: 4

ID AAB12705 standard; peptide; 4 AA.
XX
AC AAB12705;
XX
DT 22-NOV-2000 (first entry)
XX
DE Tetrapeptide messase sequence of alpha-MSH.
XX
KW Metallopeptide; combinatorial library; peptidomimetic; screening;
KW metal ion binding region; orthogonal sulphur protecting group;
KW specificity; affinity; identification; characterisation.
XX
OS Synthetic.
XX
PN WO200036136-A1.
XX
PD 22-JUN-2000.
XX
PF 14-DEC-1999; 99WO-US29743.
XX
PR 14-DEC-1998; 98US-0112235.
XX
PA (PALA-) PALATIN TECHNOLOGIES INC.
XX
PI Sharma SD, Shi Y;
XX
DR WPI; 2000-442392/38.
XX
PT New metallopeptide or metallopeptidomimetic combinatorial libraries,
PT useful for identifying agents which bind a target molecule or mediate a
PT biological activity -
XX
PS Example 5; Page 26; 55pp; English.
XX
CC The present invention describes metallopeptide combinatorial libraries
CC which are synthesised using a sequence of 2 or more amino acids
CC containing at least one S to form a metal ion-binding domain. Methods
CC from the present invention can be used for providing metallopeptide or
CC metallopeptidomimetic combinatorial libraries. In each of the methods
CC and libraries provided, a specific conformational restriction is
CC obtained upon complexing the peptides or amino acid sequences with a
CC metal ion, such that the conformationally constrained peptide-metal ion
CC complexes can serve as surrogates for reverse turn structures, such as
CC beta turns and gamma turns commonly found in naturally occurring
CC peptides and proteins. The turns formed as a consequence of metal ion
CC complexation are more stable than the naturally occurring turn
CC structures, which are stabilised only by weaker interactions such as
CC Van der Walls' interactions and hydrogen bonds. The libraries can be
CC used for the identification and characterisation of library
CC constituents which are capable of binding a target molecule of
CC interest, or mediating a biological activity of interest. The present
CC sequence represents a peptide which is used in an example from the
CC present invention.
XX
SQ Sequence 4 AA;

AAB12705 Length: 4 September 17, 2003 13:08 Type: P Check: 806 ..
Found using 'cterm' (kam547.key)

```
        |--|
1       HFRW
        1  4
```

---
1 match found in sequence:
aab29202 ; Melanocortin receptor ligand cyclic peptide analogue #2.
(from "ctermags.pep")
TOIG of: aab29202 check: 806 from: 1 to: 4

ID AAB29202 standard; Peptide; 4 AA.
XX
AC AAB29202;
XX

```
AAB11847  Length: 6  September 17, 2003 13:08  Type: P  Check: 1654  ..
Found using 'cterm' (kam547.key)

          |--|
1       XEHFRW
          3  6

-------
1 match found in sequence:
aab11848 ; Alpha-MSH analogue peptide #4.
 (from "ctermags.pep")
 TOIG of: aab11848  check: 1655  from: 1  to: 6

ID   AAB11848 standard; peptide; 6 AA.
XX
AC   AAB11848;
XX
DT   14-NOV-2000  (first entry)
XX
DE   Alpha-MSH analogue peptide #4.
XX
KW   Alpha-MSH; alpha melanocyte stimulating hormone; POMC;
KW   proopiomelanocortin peptide; peripheral energy homeostasis;
KW   lipid mobilisation; lipolysis; lipid sequestration; body weight disorder;
KW   obesity; cachexia; anorexia; bulimia; wasting disorder; cancer;
KW   cardiovascular disease; type II diabetes; atypical depression;
KW   heart failure; immune system weakness; reproductive disorder;
KW   amenorrhoea; side effect.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "N-terminal acetyl"
FT   Misc-difference 3
FT                   /note= "Optionally D-form residue"
FT   Misc-difference 4
FT                   /note= "Optionally D-form residue; D-Phe is optionally
FT                          substituted in the para position with a nitro
FT                          group"
FT   Misc-difference 5
FT                   /note= "Optionally D-form residue"
FT   Modified-site   6
FT                   /note= "C-terminal amide; optionally D-form residue"
XX
PN   WO200033658-A1.
XX
PD   15-JUN-2000.
XX
PF   09-DEC-1999;   99WO-US29337.
XX
PR   09-DEC-1998;   98US-0111581.
PR   29-JUL-1999;   99US-0146299.
PR   29-JUL-1999;   99US-0146300.
PR   29-JUL-1999;   99US-0146301.
PR   29-JUL-1999;   99US-0146302.
PR   29-JUL-1999;   99US-0146303.
PR   29-JUL-1999;   99US-0146304.
PR   29-JUL-1999;   99US-0146305.
PR   29-JUL-1999;   99US-0146306.
PR   12-AUG-1999;   99US-0374827.
XX
PA   (ROOS-) ROOSEVELT INST ELEANOR.
PA   (OKLA-) OKLAHOMA MEDICAL RES FOUND.
XX
PI   Brennan MB,  Hochgeschwender U;
XX
DR   WPI; 2000-423155/36.
XX
PT   Regulating metabolism with pro-opiomelanocortin compounds, useful e.g.
PT   for treating obesity, administered peripherally to minimize effects on
PT   the central nervous system  -
XX
PS   Claim 32d; Page -; 168pp; English.
XX
CC   The invention relates to methods and compositions for the regulation of
CC   body weight, and for the treatment of associated disorders, comprising
CC   the administration of a proopiomelanocortin (POMC) compound to
CC   peripheral tissues such that delivery to the central nervous system is
CC   minimised. The amount of POMC compound used is insufficient to alter
CC   appetite and is preferably in the range 0.1 microgram-10 mg/kg. The
CC   primary aim of the invention is therefore to effect weight regulation via
CC   the control of the lipid mobilisation and sequestration in adipose tissue
CC   (peripheral pathways of energy homeostasis) rather than via appetite
CC   modification (central pathways of energy homeostasis). The POMC compounds
CC   of the invention regulate fat stores in adipose tissue by altering free
CC   fatty acid uptake and/or lipolysis. The compounds can be used to treat
CC   or prevent disorders of body weight such as obesity, anorexia, bulimia,
CC   cachexia and wasting disorders. They can be used to treat disorders that
CC   can be associated with obesity (such as cardiovascular disease, certain
CC   cancers, type II diabetes and atypical depression), and disorders that
CC   can be associated with low body weight (such as heart failure, immune
CC   system weakness, amenorrhoea and depression). They can also be used to
CC   treat reproductive disorders and the undesirable body weight changes
CC   that can be side effects of certain pharmaceuticals. The compounds of
CC   the invention include melanocyte stimulatory hormone (MSH) analogues.
CC   MSH agonists reduce body weight, while MSH antagonists increase body
CC   weight. The invention provides alpha-MSH peptide analogues
CC   (AAB11841-B11886) and also discloses a Pomc knockout mouse for the study
CC   of peripheral and central energy homeostasis pathways. The present
CC   sequence represents an alpha-MSH analogue of the invention.
CC   Note: This sequence is not given in full in the specification, but
CC   is derived from the information provided on page 137 (claim 32d).
XX
SQ   Sequence   6 AA;

AAB11848  Length: 6  September 17, 2003 13:08  Type: P  Check: 1655  ..
Found using 'cterm' (kam547.key)

          |--|
1       YEHFRW
          3  6

-------
1 match found in sequence:
aab11862 ; [Nle4, D-Phe7]-alpha-MSH(4-9).
 (from "ctermags.pep")
 TOIG of: aab11862  check: 1654  from: 1  to: 6

ID   AAB11862 standard; peptide; 6 AA.
XX
AC   AAB11862;
XX
DT   14-NOV-2000  (first entry)
XX
DE   [Nle4, D-Phe7]-alpha-MSH(4-9).
XX
KW   Alpha-MSH; alpha melanocyte stimulating hormone; human; POMC;
KW   proopiomelanocortin peptide; peripheral energy homeostasis;
KW   lipid mobilisation; lipolysis; lipid sequestration; body weight disorder;
KW   obesity; cachexia; anorexia; bulimia; wasting disorder; cancer;
KW   cardiovascular disease; type II diabetes; atypical depression;
KW   heart failure; immune system weakness; reproductive disorder;
KW   amenorrhoea; side effect.
XX
OS   Synthetic.
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /label= Nle
FT   Misc-difference 4
FT                   /note= "D-form residue"
XX
PN   WO200033658-A1.
XX
```

```
DR   WPI; 2000-423155/36.
XX
PT   Regulating metabolism with pro-opiomelanocortin compounds, useful e.g.
PT   for treating obesity, administered peripherally to minimize effects on
PT   the central nervous system  -
XX
PS   Claim 32d; Page -; 168pp; English.
XX
CC   The invention relates to methods and compositions for the regulation of
CC   body weight, and for the treatment of associated disorders, comprising
CC   the administration of a proopiomelanocortin (POMC) compound to
CC   peripheral tissues such that delivery to the central nervous system is
CC   minimised. The amount of POMC compound used is insufficient to alter
CC   appetite and is preferably in the range 0.1 microgram-10 mg/kg. The
CC   primary aim of the invention is therefore to effect weight regulation via
CC   the control of the lipid mobilisation and sequestration in adipose tissue
CC   (peripheral pathways of energy homeostasis) rather than via appetite
CC   modification (central pathways of energy homeostasis). The POMC compounds
CC   of the invention regulate fat stores in adipose tissue by altering free
CC   fatty acid uptake and/or lipolysis. The compounds can be used to treat
CC   or prevent disorders of body weight such as obesity, anorexia, bulimia,
CC   cachexia and wasting disorders. They can be used to treat disorders that
CC   can be associated with obesity (such as cardiovascular disease, certain
CC   cancers, type II diabetes and atypical depression), and disorders that
CC   can be associated with low body weight (such as heart failure, immune
CC   system weakness, amenorrhoea and depression). They can also be used to
CC   treat reproductive disorders and the undesirable body weight changes
CC   that can be side effects of certain pharmaceuticals. The compounds of
CC   the invention include melanocyte stimulatory hormone (MSH) analogues.
CC   MSH agonists reduce body weight, while MSH antagonists increase body
CC   weight. The invention provides alpha-MSH peptide analogues
CC   (AAB11841-B11886) and also discloses a Pomc knockout mouse for the study
CC   of peripheral and central energy homeostasis pathways. The present
CC   sequence represents an alpha-MSH analogue of the invention.
CC   Note: This sequence is not given in full in the specification, but
CC   is derived from the information provided on page 137 (claim 32d).
XX
SQ   Sequence   6 AA;

 AAB11846  Length: 6  September 17, 2003 13:08  Type: P  Check: 1643  ..
 Found using 'cterm' (kam547.key)

          |--|
1       MEHFRW
          3  6

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1 match found in sequence:
 aab11847 ; Alpha-MSH analogue peptide #3.
  (from "ctermags.pep")
  TOIG of: aab11847  check: 1654  from: 1  to: 6

 ID   AAB11847 standard; peptide; 6 AA.
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 AC   AAB11847;
 XX
 DT   14-NOV-2000  (first entry)
 XX
 DE   Alpha-MSH analogue peptide #3.
 XX
 KW   Alpha-MSH; alpha melanocyte stimulating hormone; POMC;
 KW   proopiomelanocortin peptide; peripheral energy homeostasis;
 KW   lipid mobilisation; lipolysis; lipid sequestration; body weight disorder;
 KW   obesity; cachexia; anorexia; bulimia; wasting disorder; cancer;
 KW   cardiovascular disease; type II diabetes; atypical depression;
 KW   heart failure; immune system weakness; reproductive disorder;
 KW   amenorrhoea; side effect.
 XX
 OS   Synthetic.
 XX
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 FT   Misc-difference 3
 FT                   /note= "Optionally D-form residue"
 FT   Misc-difference 4
 FT                   /note= "Optionally D-form residue; D-Phe is optionally
 FT                    substituted in the para position with a nitro
 FT                    group"
 FT   Misc-difference 5
 FT                   /note= "Optionally D-form residue"
 FT   Modified-site   6
 FT                   /note= "C-terminal amide; optionally D-form residue"
 XX
 PN   WO200033658-A1.
 XX
 PD   15-JUN-2000.
 XX
 PF   09-DEC-1999;   99WO-US29337.
 XX
 PR   09-DEC-1998;   98US-0111581.
 PR   29-JUL-1999;   99US-0146299.
 PR   29-JUL-1999;   99US-0146300.
 PR   29-JUL-1999;   99US-0146301.
 PR   29-JUL-1999;   99US-0146302.
 PR   29-JUL-1999;   99US-0146303.
 PR   29-JUL-1999;   99US-0146304.
 PR   29-JUL-1999;   99US-0146305.
 PR   29-JUL-1999;   99US-0146306.
 PR   12-AUG-1999;   99US-0374827.
 XX
 PA   (ROOS-) ROOSEVELT INST ELEANOR.
 PA   (OKLA-) OKLAHOMA MEDICAL RES FOUND.
 XX
 PI   Brennan MB,  Hochgeschwender U;
 XX
 DR   WPI; 2000-423155/36.
 XX
 PT   Regulating metabolism with pro-opiomelanocortin compounds, useful e.g.
 PT   for treating obesity, administered peripherally to minimize effects on
 PT   the central nervous system  -
 XX
 PS   Claim 32d; Page -; 168pp; English.
 XX
 CC   The invention relates to methods and compositions for the regulation of
 CC   body weight, and for the treatment of associated disorders, comprising
 CC   the administration of a proopiomelanocortin (POMC) compound to
 CC   peripheral tissues such that delivery to the central nervous system is
 CC   minimised. The amount of POMC compound used is insufficient to alter
 CC   appetite and is preferably in the range 0.1 microgram-10 mg/kg. The
 CC   primary aim of the invention is therefore to effect weight regulation via
 CC   the control of the lipid mobilisation and sequestration in adipose tissue
 CC   (peripheral pathways of energy homeostasis) rather than via appetite
 CC   modification (central pathways of energy homeostasis). The POMC compounds
 CC   of the invention regulate fat stores in adipose tissue by altering free
 CC   fatty acid uptake and/or lipolysis. The compounds can be used to treat
 CC   or prevent disorders of body weight such as obesity, anorexia, bulimia,
 CC   cachexia and wasting disorders. They can be used to treat disorders that
 CC   can be associated with obesity (such as cardiovascular disease, certain
 CC   cancers, type II diabetes and atypical depression), and disorders that
 CC   can be associated with low body weight (such as heart failure, immune
 CC   system weakness, amenorrhoea and depression). They can also be used to
 CC   treat reproductive disorders and the undesirable body weight changes
 CC   that can be side effects of certain pharmaceuticals. The compounds of
 CC   the invention include melanocyte stimulatory hormone (MSH) analogues.
 CC   MSH agonists reduce body weight, while MSH antagonists increase body
 CC   weight. The invention provides alpha-MSH peptide analogues
 CC   (AAB11841-B11886) and also discloses a Pomc knockout mouse for the study
 CC   of peripheral and central energy homeostasis pathways. The present
 CC   sequence represents an alpha-MSH analogue of the invention.
 CC   Note: This sequence is not given in full in the specification, but
 CC   is derived from the information provided on page 137 (claim 32d).
 XX
 SQ   Sequence   6 AA;
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KW   amenorrhoea; side effect.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
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FT                   /note= "N-terminal acetyl"
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FT                   /note= "Optionally D-form residue; D-Phe is optionally
FT                          substituted in the para position with a nitro
FT                          group"
FT   Misc-difference 4
FT                   /note= "Optionally D-form residue"
FT   Modified-site   5
FT                   /note= "C-terminal amide; optionally D-form residue"
XX
PN   WO200033658-A1.
XX
PD   15-JUN-2000.
XX
PF   09-DEC-1999;   99WO-US29337.
XX
PR   09-DEC-1998;   98US-0111581.
PR   29-JUL-1999;   99US-0146299.
PR   29-JUL-1999;   99US-0146300.
PR   29-JUL-1999;   99US-0146301.
PR   29-JUL-1999;   99US-0146302.
PR   29-JUL-1999;   99US-0146303.
PR   29-JUL-1999;   99US-0146304.
PR   29-JUL-1999;   99US-0146305.
PR   29-JUL-1999;   99US-0146306.
PR   12-AUG-1999;   99US-0374827.
XX
PA   (ROOS-) ROOSEVELT INST ELEANOR.
PA   (OKLA-) OKLAHOMA MEDICAL RES FOUND.
XX
PI   Brennan MB,  Hochgeschwender U;
XX
DR   WPI; 2000-423155/36.
XX
PT   Regulating metabolism with pro-opiomelanocortin compounds, useful e.g.
PT   for treating obesity, administered peripherally to minimize effects on
PT   the central nervous system -
XX
PS   Claim 32d; Page -; 168pp; English.
XX
CC   The invention relates to methods and compositions for the regulation of
CC   body weight, and for the treatment of associated disorders, comprising
CC   the administration of a proopiomelanocortin (POMC) compound to
CC   peripheral tissues such that delivery to the central nervous system is
CC   minimised. The amount of POMC compound used is insufficient to alter
CC   appetite and is preferably in the range 0.1 microgram-10 mg/kg. The
CC   primary aim of the invention is therefore to effect weight regulation via
CC   the control of the lipid mobilisation and sequestration in adipose tissue
CC   (peripheral pathways of energy homeostasis) rather than via appetite
CC   modification (central pathways of energy homeostasis). The POMC compounds
CC   of the invention regulate fat stores in adipose tissue by altering free
CC   fatty acid uptake and/or lipolysis. The compounds can be used to treat
CC   or prevent disorders of body weight such as obesity, anorexia, bulimia,
CC   cachexia and wasting disorders. They can be used to treat disorders that
CC   can be associated with obesity (such as cardiovascular disease, certain
CC   cancers, type II diabetes and atypical depression), and disorders that
CC   can be associated with low body weight (such as heart failure, immune
CC   system weakness, amenorrhoea and depression). They can also be used to
CC   treat reproductive disorders and the undesirable body weight changes
CC   that can be side effects of certain pharmaceuticals. The compounds of
CC   the invention include melanocyte stimulatory hormone (MSH) analogues.
CC   MSH agonists reduce body weight, while MSH antagonists increase body
CC   weight. The invention provides alpha-MSH peptide analogues
CC   (AAB11841-B11886) and also discloses a Pomc knockout mouse for the study
CC   of peripheral and central energy homeostasis pathways. The present
CC   sequence represents an alpha-MSH analogue of the invention.
CC   Note: This sequence is not given in full in the specification, but
CC   is derived from the information provided on page 137 (claim 32d).
XX
SQ   Sequence   5 AA;

AAB11845  Length: 5  September 17, 2003 13:08  Type: P  Check: 1188  ..
Found using 'cterm' (kam547.key)

        |--|
1       GHFRW
         2  5

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1 match found in sequence:
aab11846 ; Alpha-MSH analogue peptide #2.
 (from "ctermags.pep")
 TOIG of: aab11846  check: 1643  from: 1  to: 6

ID   AAB11846 standard; peptide; 6 AA.
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AC   AAB11846;
XX
DT   14-NOV-2000  (first entry)
XX
DE   Alpha-MSH analogue peptide #2.
XX
KW   Alpha-MSH; alpha melanocyte stimulating hormone; POMC;
KW   proopiomelanocortin peptide; peripheral energy homeostasis;
KW   lipid mobilisation; lipolysis; lipid sequestration; body weight disorder;
KW   obesity; cachexia; anorexia; bulimia; wasting disorder; cancer;
KW   cardiovascular disease; type II diabetes; atypical depression;
KW   heart failure; immune system weakness; reproductive disorder;
KW   amenorrhoea; side effect.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "N-terminal acetyl"
FT   Misc-difference 3
FT                   /note= "Optionally D-form residue"
FT   Misc-difference 4
FT                   /note= "Optionally D-form residue; D-Phe is optionally
FT                          substituted in the para position with a nitro
FT                          group"
FT   Misc-difference 5
FT                   /note= "Optionally D-form residue"
FT   Modified-site   6
FT                   /note= "C-terminal amide; optionally D-form residue"
XX
PN   WO200033658-A1.
XX
PD   15-JUN-2000.
XX
PF   09-DEC-1999;   99WO-US29337.
XX
PR   09-DEC-1998;   98US-0111581.
PR   29-JUL-1999;   99US-0146299.
PR   29-JUL-1999;   99US-0146300.
PR   29-JUL-1999;   99US-0146301.
PR   29-JUL-1999;   99US-0146302.
PR   29-JUL-1999;   99US-0146303.
PR   29-JUL-1999;   99US-0146304.
PR   29-JUL-1999;   99US-0146305.
PR   29-JUL-1999;   99US-0146306.
PR   12-AUG-1999;   99US-0374827.
XX
PA   (ROOS-) ROOSEVELT INST ELEANOR.
PA   (OKLA-) OKLAHOMA MEDICAL RES FOUND.
XX
PI   Brennan MB,  Hochgeschwender U;
XX
```

```
> O <
O| |O  IntelliGenetics
> O <

Quest - Quick User-directed Expression Search Tool
Release 5.4

                -- Outline of search "cterm_ags" --

Selected search type is key against sequence data banks or files.
Selected scope is Sequence.
Selected sequence key from "kam547.key":
  cterm (AA) ID   cterm AA preliminary pattern
1       hfrw

Selected files:

        File : ctermags.pep

                    -- Output Parameters --

Format Options:                         File Options:
  Nucleic acid code matching   Exact     Indirect file              No
  Find non-matching hits only  No        Sequence or key file       No
  Report key used              Yes       List of hits               Yes
  Note position of hit         Yes       Hit display                Yes
  Display full annotations     Yes       Name and annotations       Yes
  Sequence context             50


                    -- Run Parameters --

  Run mode                     Batch
    Time to start comparison   now
    Notify at end of run       No

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  (from "ctermags.pep")
  TOIG of: aab11839  check: 1186  from: 1  to: 5

 ID   AAB11839 standard; peptide; 5 AA.
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 AC   AAB11839;
 XX
 DT   14-NOV-2000  (first entry)
 XX
 DE   Proopiomelanocortin (POMC)-derived peptide, SEQ ID NO:1.
 XX
 KW   Proopiomelanocortin peptide; POMC; peripheral energy homeostasis;
 KW   lipid mobilisation; lipolysis; lipid sequestration; body weight disorder;
 KW   obesity; cachexia; anorexia; bulimia; wasting disorder; cancer;
 KW   cardiovascular disease; type II diabetes; atypical depression;
 KW   heart failure; immune system weakness; reproductive disorder;
 KW   amenorrhoea; side effect.
 XX
 OS   Unidentified.
 XX
 PN   WO200033658-A1.
 XX
 PD   15-JUN-2000.
 XX
 PF   09-DEC-1999;   99WO-US29337.
 XX
 PR   09-DEC-1998;   98US-0111581.
 PR   29-JUL-1999;   99US-0146299.
 PR   29-JUL-1999;   99US-0146300.
 PR   29-JUL-1999;   99US-0146301.
 PR   29-JUL-1999;   99US-0146302.
 PR   29-JUL-1999;   99US-0146303.
 PR   29-JUL-1999;   99US-0146304.
 PR   29-JUL-1999;   99US-0146305.
 PR   29-JUL-1999;   99US-0146306.
 PR   12-AUG-1999;   99US-0374827.
 XX
 PA   (ROOS-) ROOSEVELT INST ELEANOR.
 PA   (OKLA-) OKLAHOMA MEDICAL RES FOUND.
 XX
 PI   Brennan MB,  Hochgeschwender U;
 XX
 DR   WPI; 2000-423155/36.
 XX
 PT   Regulating metabolism with pro-opiomelanocortin compounds, useful e.g.
 PT   for treating obesity, administered peripherally to minimize effects on
 PT   the central nervous system  -
 XX
 PS   Disclosure; Page 40; 168pp; English.
 XX
 CC   The invention relates to methods and compositions for the regulation of
 CC   body weight, and for the treatment of associated disorders, comprising
 CC   the administration of a proopiomelanocortin (POMC) compound to
 CC   peripheral tissues such that delivery to the central nervous system is
 CC   minimised. The amount of POMC compound used is insufficient to alter
 CC   appetite and is preferably in the range 0.1 microgram-10 mg/kg. The
 CC   primary aim of the invention is therefore to effect weight regulation via
 CC   the control of the lipid mobilisation and sequestration in adipose tissue
 CC   (peripheral pathways of energy homeostasis) rather than via appetite
 CC   modification (central pathways of energy homeostasis). The POMC compounds
 CC   of the invention regulate fat stores in adipose tissue by altering free
 CC   fatty acid uptake and/or lipolysis. The compounds can be used to treat
 CC   or prevent disorders of body weight such as obesity, anorexia, bulimia,
 CC   cachexia and wasting disorders. They can be used to treat disorders that
 CC   can be associated with obesity (such as cardiovascular disease, certain
 CC   cancers, type II diabetes and atypical depression), and disorders that
 CC   can be associated with low body weight (such as heart failure, immune
 CC   system weakness, amenorrhoea and depression). They can also be used to
 CC   treat reproductive disorders and the undesirable body weight changes
 CC   that can be side effects of certain pharmaceuticals. The compounds of
 CC   the invention include melanocyte stimulatory hormone (MSH) analogues.
 CC   MSH agonists reduce body weight, while MSH antagonists increase body
 CC   weight. The invention provides alpha-MSH peptide analogues
 CC   (AAB11841-B11886) and also discloses a Pomc knockout mouse for the study
 CC   of peripheral and central energy homeostasis pathways. The present
 CC   sequence represents a POMC-derived peptide. Peptides containing this
 CC   motif may be used according to the invention.
 XX
 SQ   Sequence   5 AA;

 AAB11839  Length: 5  September 17, 2003 13:08  Type: P  Check: 1186  ..
 Found using 'cterm' (kam547.key)

         |--|
1       EHFRW
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1 match found in sequence:
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  (from "ctermags.pep")
  TOIG of: aab11845  check: 1188  from: 1  to: 5

 ID   AAB11845 standard; peptide; 5 AA.
 XX
 AC   AAB11845;
 XX
 DT   14-NOV-2000  (first entry)
 XX
 DE   Alpha-MSH analogue peptide #1.
 XX
 KW   Alpha-MSH; alpha melanocyte stimulating hormone; POMC;
 KW   proopiomelanocortin peptide; peripheral energy homeostasis;
 KW   lipid mobilisation; lipolysis; lipid sequestration; body weight disorder;
 KW   obesity; cachexia; anorexia; bulimia; wasting disorder; cancer;
 KW   cardiovascular disease; type II diabetes; atypical depression;
 KW   heart failure; immune system weakness; reproductive disorder;
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Kam 10/040,547

```
=> d his 1

     (FILE 'HCAPLUS' ENTERED AT 15:43:47 ON 17 SEP 2003)
L18          84 S L8 OR L14-L17

=> d que l18
L1          160 SEA FILE=REGISTRY HFRW^/SQSP
L2          161 SEA FILE=HCAPLUS L1
L3           64 SEA FILE=HCAPLUS L2 AND MSH
L4           21 SEA FILE=HCAPLUS L2 AND MELANOCYTE#
L5           35 SEA FILE=HCAPLUS L2 AND MELANOCORTIN#
L6           77 SEA FILE=HCAPLUS L3 OR L4 OR L5
L7            8 SEA FILE=HCAPLUS L2 AND SEXUAL?
L8           78 SEA FILE=HCAPLUS L6 OR L7
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L10          19 SEA FILE=HCAPLUS SHADIACK A?/AU
L11         868 SEA FILE=HCAPLUS BERNSTEIN J?/AU
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L15           6 SEA FILE=HCAPLUS L13 AND MELANOCORTIN#
L16           0 SEA FILE=HCAPLUS L13 AND MELANOCYTE#
L17           6 SEA FILE=HCAPLUS L13 AND SEXUAL?
L18          84 SEA FILE=HCAPLUS L8 OR (L14 OR L15 OR L16 OR L17)


=> d ibib abs l18 1-84

L18  ANSWER 1 OF 84  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:610481  HCAPLUS
DOCUMENT NUMBER:          139:133842
TITLE:                    Preparation of novel peptide derivatives and their
                          therapeutic and cosmetic application
INVENTOR(S):              Pinel, Anne-Marie
PATENT ASSIGNEE(S):       Institut Europeen de Biologie Cellulaire, Fr.
SOURCE:                   PCT Int. Appl., 27 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
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     WO 2003064458      A2   20030807       WO 2003-FR300     20030131
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
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             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
             ML, MR, NE, SN, TD, TG
     FR 2835528         A1   20030808       FR 2002-1202      20020201
PRIORITY APPLN. INFO.:                   FR 2002-1202      A   20020201
OTHER SOURCE(S):          MARPAT 139:133842
```

Search completed by David Schreiber 308-4292

AB The invention relates to peptides R-V-Ala-His-X-Y-Trp5-NH2 [R is H or a protective group chosen from benzoyl, tosyl, benzenesulfonyl, benzyloxycarbonyl, or pyridinepropionyl; V is a natural or unnatural amino acid chosen from norleucine, norvaline, or 2-N-methylnorleucine; X is a natural or nonnatural D- or L-amino acid having arom. character chosen from phenylalanine, 1- or 2-naphthylalanine, phenylglycine, benzothienylalanine, 4,4'-biphenylalanine, 3,3-diphenylalanine, homophenylalanine, indanylglycine, 4-methylphenylalanine, thienylalanine, p-nitrophenylalanine, or halophenylalanine; Y is a natural or unnatural amino acid of L-configuration having basic character chosen from arginine, lysine, or ornithine] and their enantiomers, diastereomers, or mixts. for application in the field of therapeutics or cosmetics. Thus, Ac-Nle-Ala-His-D-Phe-Arg-Trp-NH2 was prepd. by the solid phase method and assayed for prodn. of cAMP (80% in comparison with .alpha.-**MSH**).

L18 ANSWER 2 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:604743 HCAPLUS
TITLE: PT-141: a **melanocortin** agonist for the treatment of **sexual** dysfunction
AUTHOR(S): Molinoff, P. B.; **Shadiack, A. M.**; Earle, D.; Diamond, L. E.; Quon, C. Y.
CORPORATE SOURCE: Palatin Technologies, Inc., Cranbury, NJ, 08512, USA
SOURCE: Annals of the New York Academy of Sciences (2003), 994(Melanocortin System), 96-102
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PT-141, a synthetic peptide analog of .alpha.-**MSH**, is an agonist at **melanocortin** receptors including the MC3R and MC4R, which are expressed primarily in the central nervous system. Administration of PT-141 to rats and nonhuman primates results in penile erections. Systemic administration of PT-141 to rats activates neurons in the hypothalamus as shown by an increase in c-Fos immunoreactivity. Neurons in the same region of the central nervous system take up pseudorabies virus injected into the corpus cavernosum of the rat penis. Administration of PT-141 to normal men and to patients with erectile dysfunction resulted in a rapid dose-dependent increase in erectile activity. The results suggest that PT-141 holds promise as a new treatment for **sexual** dysfunction.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:438971 HCAPLUS
DOCUMENT NUMBER: 139:144389
TITLE: Physiologic effect of leptin on insulin secretion is mediated mainly through central mechanisms
AUTHOR(S): Muzumdar, Radhika; Ma, Xiaohui; Yang, Xiaoman; Atzmon, Gil; **Bernstein, Julia**; Karkanias, George; Barzilai, Nir
CORPORATE SOURCE: Institute for Aging Research, Department of Medicine, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SOURCE: FASEB Journal (2003), 17(9), 1130-1132, 10.1096/fj.02-0991fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology

Search completed by David Schreiber 308-4292

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Leptin has been shown to decrease glucose-stimulated insulin secretion in both in vivo and in vitro studies. As some of the effects of leptin have been elicited through both peripheral and central mechanisms, we assessed whether leptin modulates insulin secretion also through the central nervous system. We infused leptin or saline through implanted intracerebroventricular (ICV) catheters to chronically catheterized, conscious rats, 2 h after initiation of hyperglycemic (.apprx.11 mM) clamp. On ICV administration of leptin, there was a gradual and progressive decrease in plasma insulin levels by 52% with 30 ng and by 28% with 20 ng of leptin compared with ICV saline. The effect of 20 ng leptin ICV was replicated by i.v. leptin infusion that achieved physiol. leptin levels of .apprx.17 ng/mL. When the **melanocortin** (MC) pathway was blocked with a nonselective MC-3/4 antagonist SHU 9119 administered ICV, and either saline or leptin was infused i.v., leptin failed to produce a decrease in glucose-stimulated insulin levels. We conclude that leptin decreases insulin levels by a predominantly central mechanism, probably via the **melanocortin** receptors; and peripheral leptin receptors on the .beta. cells do not play a major role. The physiol. features of this response suggest a possible role for leptin in the evolution of diabetes in overweight individuals.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:249767 HCAPLUS
DOCUMENT NUMBER: 139:95624
TITLE: Discovery and in vivo evaluation of new **melanocortin**-4 receptor-selective peptides
AUTHOR(S): Nijenhuis, Wouter A. J.; Kruijtzer, John A. W.; Wanders, Nienke; Vrinten, Dorien H.; Garner, Keith M.; Schaaper, Wim M. M.; Meloen, Rob H.; Gispen, Willem Hendrik; Liskamp, Rob M.; Adan, Roger A. H.
CORPORATE SOURCE: Rudolf Magnus Institute of Neuroscience, Department of Pharmacology and Anatomy, University Medical Center Utrecht, Utrecht, 3584 CG, Neth.
SOURCE: Peptides (New York, NY, United States) (2003), 24(2), 271-280
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **melanocortin**-4 receptor (MC4R) is involved in several physiol. processes, including body wt. regulation and grooming behavior in rats. It has also been suggested that the MC4R mediates the effects of **melanocortin** ligands on neuropathic pain. Selective compds. are needed to study the exact role of the MC4R in these different processes. The authors describe here the development and evaluation of new **melanocortin** compds. that are selective for the MC4R as compared with the other centrally expressed receptors, MC3R and MC5R. First, a library of 18 peptides, in which a **melanocortin**-based sequence was systematically point-mutated, was screened for binding to and activity on the MC3R, MC4R and MC5R. Compd. Ac-Nle-Gly-Lys-d-Phe-Arg-Trp-Gly-NH2 (JK1) appeared to be the most selective MC4R compd., based on affinity. This compd. is 90- and 110-fold selective for the MC4R as compared to the MC3R and MC5R, resp. Subsequent modification of JK1 yielded compd. Ac-Nle-Gly-Lys-d-Nal(2)-Arg-Trp-Gly-NH2 (JK7), a selective MC4R antagonist with 34-fold MC4R/MC3R and 109-fold MC4R/MC5R selectivity. The compds.

were active in vivo as detd. in a grooming assay and a model for neuropathic pain in rats. I.v. (i.v.) injections suggested that they were able to pass the blood-brain barrier. The compds. identified here will be useful in further research on the physiol. roles of the MC4R.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:217986 HCAPLUS
DOCUMENT NUMBER: 138:238445
TITLE: **Melanocortin** receptor-3 ligands for treating **sexual** dysfunction
INVENTOR(S): Dines, Kevin C.; Gahman, Timothy C.; Girten, Beverly E.; Hitchin, Douglas L.; Holme, Kevin R.; Lang, Hengyuan; Slivka, Sandra R.; Watson-Straughan, Karen J.; Tuttle, Ronald R.; Pei, Yazhong
PATENT ASSIGNEE(S): Lion Bioscience AG, Germany
SOURCE: U.S., 25 pp., Cont.-in-part of U.S. Ser. No. 364,825, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6534503	B1	20030318	US 2000-615479	20000713
US 6127381	A	20001003	US 1999-301391	19990428
US 6608082	B1	20030819	US 1999-306686	19990506
US 6284735	B1	20010904	US 1999-356386	19990716

PRIORITY APPLN. INFO.:
US 1998-83368P P 19980428
US 1999-301391 A1 19990428
US 1999-306686 A2 19990506
US 1999-356386 A2 19990716
US 1999-364825 B2 19990730
US 1999-401004 A2 19990921

OTHER SOURCE(S): MARPAT 138:238445
AB Methods are described for treating **sexual** dysfunction, such as erectile dysfunction or **sexual** arousal disorder, with peptides having the sequence -D-Phe-Arg-D-Trp-. A particularly useful compd. is HP-228 (Ac-Nle-Gln-His-D-Phe-Arg-D-Trp-Gly-NH2), which was prepd. by the solid-phase method and assayed for biol. activity. The invention also provides methods for selecting **melanocortin** receptor-3 ligands by detg. whether a compd. modulates the activity of MC-3 as an agonist or antagonist. These methods can be used to screen compd. libraries (e.g., benzimidazole derivs., which are claimed) for ligands to treat MC-3-assocd. conditions.
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:126689 HCAPLUS
DOCUMENT NUMBER: 138:379360
TITLE: Characterization of aliphatic, cyclic, and aromatic N-terminally "capped" His-D-Phe-Arg-Trp-NH2 tetrapeptides at the **melanocortin** receptors
AUTHOR(S): Holder, Jerry Ryan; Marques, Fernanda F.; Xiang, Zhimin; Bauzo, Rayna M.; Haskell-Luevano, Carrie

CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610-0485, USA
SOURCE: European Journal of Pharmacology (2003), 462(1-3), 41-52
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **melanocortin** system is implicated in multiple physiol. pathways including pigmentation, inflammation, erectile function, feeding behavior, energy homeostasis, wt. homeostasis, and exocrine gland function, just to list a few. The endogenous agonists for the **melanocortin** receptors include the gene transcripts derived from the proopiomelanocortin gene and include the core tetrapeptide His-Phe-Arg-Trp sequence postulated to be important for **melanocortin** receptor selectivity and stimulation. Posttranslational processing of the proopiomelanocortin derived agonists results in the N-terminal acetylation and C-terminal amidation of .alpha.-**melanocyte** stimulation hormone (.alpha.-**MSH**). In this study the authors generated 25 N-terminally "capped" tetrapeptides contg. the core sequence X-His-D-Phe-Arg-Trp-NH2 and pharmacol. characterized them at the mouse **melanocortin** MC1 receptor, **melanocortin** MC3 receptor, **melanocortin** MC4 receptor, and **melanocortin** MC5 receptor. The N-terminal "capping" groups consisted of linear, cyclic, or arom. moieties and all resulted in full agonist activity at the **melanocortin** receptors examd. in this study. Increasing aliph. chain length increased potency of the tetrapeptide derivs., with the addn. of octanoyl capping group resulting in 70- to 110-fold increased tetrapeptide potency at the **melanocortin** MC1 receptor (EC50 = 0.4 nM), **melanocortin** MC3 receptor (EC50 = 4.0 nM), and **melanocortin** MC4 receptor (EC50 = 0.4 nM) while only enhancing potency at the **melanocortin** MC5 receptor (EC50 = 0.8 nM) by 8-fold, compared to the tetrapeptide His-d-Phe-Arg-Trp-NH2. This octanoyl deriv. surprisingly resulted in a 14-fold greater potency than .alpha.-**MSH** (EC50 = 5.4 nM) at the mouse **melanocortin** MC4 receptor implicated in feeding behavior and obesity. The 3,3,3-triphenylpropionyl deriv. resulted in greater than 14 .mu.M agonist potencies at the **melanocortin** MC1 receptor, **melanocortin** MC3 receptor, and **melanocortin** MC4 receptor and possessed a 140 nM agonist EC50 value at the **melanocortin** MC5 receptor. This 3,3,3-triphenylpropionyl-His-d-Phe-Arg-Trp-NH2 peptide is a 100-fold selective agonist for the **melanocortin** MC5 receptor, vs. the other **melanocortin** receptors studied herein, and is the first **melanocortin** MC5 receptor selective tetrapeptide deriv. reported to date with nanomolar potency.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:91569 HCAPLUS
DOCUMENT NUMBER: 138:396311

TITLE: Structure-activity relationships of the **melanocortin** tetrapeptide Ac-His-DPhe-Arg-Trp-NH2 at the mouse **melanocortin** receptors Part 3: modifications at the Arg position

AUTHOR(S): Holder, Jerry Ryan; Xiang, Zhimin; Bauzo, Rayna M.; Haskell-Luevano, Carrie
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610-0485, USA

SOURCE: Peptides (New York, NY, United States) (2003), 24(1), 73-82
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **melanocortin** pathway is involved in the regulation of several physiol. functions including skin pigmentation, steroidogenesis, obesity, energy homeostasis, and exocrine gland function. This **melanocortin** pathway consists of five known G-protein coupled receptors, endogenous agonists derived from the proopiomelanocortin (POMC) gene transcript, the endogenous antagonists Agouti and the Agouti-related protein (AGRP) and signals through the intracellular cAMP signal transduction pathway. The **melanocortin**-3 receptor (MC3R) and **melanocortin**-4 receptor (MC4R) located in the brain are implicated as participating in the metabolic and food intake aspects of energy homeostasis and are stimulated by **melanocortin** agonists such as .alpha.-**melanocyte** stimulation hormone (.alpha.-**MSH**). All the endogenous (POMC-derived) **melanocortin** agonists contain the putative message sequence "His-Phe-Arg-Trp". Herein, the authors report 12 tetrapeptides, based upon the template Ac-His6-D-Phe7-Arg8-Trp9-NH2 (.alpha.-**MSH** numbering) that have been modified at the Arg8 position by neutral, basic, or acidic amino acid side chains. These peptides have been pharmacol. characterized for agonist activity at the mouse **melanocortin** receptors MC1R, MC3R, MC4R, and MC5R. The most notable results of this study include the observation that removal of the guanidinyl side chain moiety results in decreased **melanocortin** receptor potency, but that this Arg8 side chain is not crit. for **melanocortin** receptor agonist activity. Addnl., incorporation of the homoArg8 residue results in 56-fold MC4R vs. MC3R selectivity, and the Orn8 residue results in 123-fold MC4R vs. MC5R and 63-fold MC5R vs. MC3R selectivity.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:58220 HCAPLUS
DOCUMENT NUMBER: 138:117676

TITLE: Linear and cyclic **melanocortin** receptor-specific peptides, and therapeutic use

INVENTOR(S): Sharma, Shubh D.; **Shadiack, Annette M.**; Yang, Wei; Rajpurohit, Ramesh
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA

SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006620	A2	20030123	WO 2002-US22196	20020711

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-304836P P 20010711
OTHER SOURCE(S): MARPAT 138:117676
AB Linear and cyclic peptides are provided which are specific to **melanocortin** receptors and which exhibit agonist, antagonist, or mixed agonist-antagonist activity. The peptides of the invention may be used to treat e.g. erectile dysfunction and eating disorders.

L18 ANSWER 9 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:965114 HCAPLUS
DOCUMENT NUMBER: 138:33375
TITLE: Methods of treating bladder disorders
INVENTOR(S): Hedley, Mary Lynne
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002193332	A1	20021219	US 2002-74956	20020212

PRIORITY APPLN. INFO.: US 2001-268175P P 20010212
AB Methods of treating bladder disorders, including bladder cancer and inflammatory bladder diseases such as interstitial cystitis are disclosed. The methods include identifying a mammal that has or is at risk for having a bladder disorder and administering isolated nucleic acid sequences to the mammal. Nucleic acids used in the methods of the invention contain unmethylated CpG sequences, which are thought to modulate the immune response. Also included are methods that use nucleic acids encoding alpha-**MSH**. The nucleic acid sequences may be administered individually or together or can be included in the same nucleic acid.

L18 ANSWER 10 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:889675 HCAPLUS
DOCUMENT NUMBER: 138:101078
TITLE: Structure-activity relationships of the **melanocortin** tetrapeptide Ac-His-D-Phe-Arg-Trp-NH2 at the mouse **melanocortin** receptors. 4. Modifications at the Trp position
AUTHOR(S): Holder, Jerry Ryan; Xiang, Zhimin; Bauzo, Rayna M.; Haskell-Luevano, Carrie
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(26), 5736-5744
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **melanocortin** pathway is involved in the regulation of several physiol. functions including skin pigmentation, steroidogenesis, obesity, energy homeostasis, and exocrine gland function. This **melanocortin** pathway consists of five known G-protein coupled

receptors, endogenous agonists derived from the proopiomelanocortin (POMC) gene transcript, the endogenous antagonists Agouti and the Agouti-related protein (AGRP) and signals through the intracellular cAMP signal transduction pathway. The endogenous **melanocortin** agonists contain the putative message sequence "His-Phe-Arg-Trp," postulated to be important for **melanocortin** receptor mol. recognition and stimulation. Herein, the authors report a tetrapeptide library, based upon the template Ac-His--D-Phe-Arg-Trp-NH2, consisting of 20 members that have been modified at the Trp9 position (.alpha.-**MSH** numbering) and pharmacol. characterized for agonist activity at the mouse **melanocortin** receptors MC1R, MC3R, MC4R, and MC5R. Results from this study yielded compds. that ranged in pharmacol. properties from equipotent to a loss of **melanocortin** receptor activity at up to 100 .mu.M concns. Interestingly, modification of the Trp9 in the tetrapeptide template at the MC1R resulted in only up to a 220-fold potency change, while at the MC4R and MC5R, up to a 9700-fold decrease in potency was obsd., suggesting the MC1R is more tolerant of the modifications examd. herein. The most notable results of this study include identification that the Trp9 indole moiety in the tetrapeptide template is important for **melanocortin**-3 receptor agonist potency, and that this position can be used to design **melanocortin** ligands possessing receptor selectivity for the peripherally expressed MC1 and MC5 vs. the centrally expressed MC3 and MC4 receptors. Specifically, the Ac-His--D-Phe-Arg-Tic-NH2 and the Ac-His--D-Phe-Arg-Bip-NH2 tetrapeptides possessed nanomolar MC1R and MC5R potency but micromolar MC3R and MC4R agonist potency. Addnl., these studies identified that substitution of the Trp amino acid with either Nal(2') or D-Nal(2') resulted in equipotent **melanocortin** receptor potency, suggesting that the chem. reactive Trp indole side chain may be replaced with the nonreactive Nal(2') moiety for the design of nonpeptide **melanocortin** receptor agonists.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

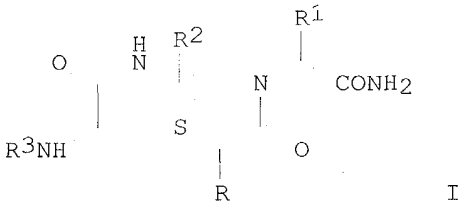
L18 ANSWER 11 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:692551 HCAPLUS
DOCUMENT NUMBER: 138:131289
TITLE: Structure-activity relationship studies (SAR) of **melanocortin** agonists central His-Phe-Arg-Trp sequence
AUTHOR(S): Holder, Jerry Ryan; Bauzo, Rayna M.; Xiang, Zhimin; Haskell-Luevano, Carrie
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610, USA
SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 706-707. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.
CODEN: 69DBAL; ISBN: 0-9715560-0-8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Sixty positionally modified tetrapeptides were synthesized, purified and characterized at the mouse **melanocortin** 4 receptor to evaluate the role of the His-Phe-Arg-Trp amino acids in receptor activity. Substitution of the four A.A. residues with alanine led to decreased receptor activity. The chirality of positions 6,7, and 9 is significant for activity at the MC4R.

Search completed by David Schreiber 308-4292

Kam 10/040;547

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:640914 HCAPLUS
DOCUMENT NUMBER: 137:325634
TITLE: A Solid-Phase Approach to Mouse **Melanocortin** Receptor Agonists Derived from a Novel Thioether Cyclized Peptidomimetic Scaffold
AUTHOR(S): Bondebjerg, Jon; Xiang, Zhimin; Bauzo, Rayna M.; Haskell-Luevano, Carrie; Meldal, Morten
CORPORATE SOURCE: Department of Chemistry, Carlsberg Laboratory, Valby, DK-2500, Den.
SOURCE: Journal of the American Chemical Society (2002), 124(37), 11046-11055
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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AB The solid-phase synthesis of novel thioether cyclized peptidomimetics I [R = H, Ph; R1 = 1-naphthylmethyl, 3-indolylmethyl, CH2Ph, CH2C6H4OH-4, (CH2)3NHC(:NH)NH2; R2 = (CH2)4NH2, (CH2)3NHC(:NH)NH2, CH2Ph, CH2CHMe2; R2 forms proline ring with adjacent NH; R3 = 1-naphthylmethyl, 2-naphthoyl, MeCO-His-D-Phe-] is reported. The thioether bridge is formed on-bead by an intramol. reaction between a chloroacetylated reduced peptide bond and the free thiol from a cysteine. The C-terminal amides in I were unstable and partially hydrolyzed to the free acids; hydrolysis could be reduced to less than 5% by using neat TFA for short periods of time (30 min) preferably using lypophilized resin. I were tested for agonist activity at the mouse **melanocortin** receptors 1, 3, 4, and 5 (mMC1-5R). Several compds. were identified as having low micromolar agonist activity at the mMC1R (involved in skin pigmentation and animal coat coloration) and mMC4R (involved in regulation of appetite and food intake). The most potent I [R = H, R1 = 3-indolylmethyl, R2 = (CH2)3NHC(:NH)NH2, R3 = MeCO-His-D-Phe-], based on the pharmacophore motif "His-DPhe-Arg-Trp", was identified as having an EC50 value of 165 nM at mMC1R, 7600 nM at mMC3R, 650 nM at mMC4R, and 335 nM at mMC5R. In addn., some of the compds. showed moderate selectivity for the mMC1R.
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 13 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:637788 HCAPLUS
DOCUMENT NUMBER: 137:179841
TITLE: Identification of target-specific folding sites in

peptides and proteins
INVENTOR(S): Sharma, Shubh D.; Shi, Yi-Qun
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064734	A2	20020822	WO 2001-US50075	20011219

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-256842P P 20001219
US 2001-304835P P 20010711
US 2001-327835P P 20011004

AB The invention provides methods for identification and detn. of target-specific folding sites in peptides and proteins, including a method for detg. a secondary structure binding to a target of interest within a known parent polypeptide that binds to the target of interest. In one embodiment of the invention, a residue or mimetic contg. a nitrogen atom and a sulfur atom available for binding to a metal ion is serially substituted for single residues in or inserted between two adjacent residues in a known primary sequence of a peptide or protein. The resulting sequence, which includes a min. of the residue or mimetic contg. a nitrogen atom and a sulfur atom available for binding to a metal ion and two residues on the amino terminus side thereof, is complexed with a metal ion, thereby forming a metallopeptide. The resulting metallopeptides are then used in binding or functional assays related to the target of interest, and the metallopeptide demonstrating binding or functional activity is selected. The invention further provides methods to det. the specific sequence and local three-dimensional structure of that portion of peptides or proteins that bind to a receptor or target of interest, or mediate a biol. activity of interest and methods to det. the pharmacophore of receptors or targets of interest. The invention provides for defined pharmacophores or receptors or targets of interest and directed libraries for identification and detn. of target-specific folding sites in peptides and proteins and for identification and detn. of pharmacophores of receptors or targets of interest.

L18 ANSWER 14 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:637480 HCAPLUS
DOCUMENT NUMBER: 137:190724
TITLE: **Melanocortin** metallopeptides for treatment of **sexual** dysfunction
INVENTOR(S): Sharma, Shubh D.; Shi, Yi-qun; Yang, Wei; Cai, Hui-zhi; **Shadiack, Annette**
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2

Search completed by David Schreiber 308-4292

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064091	A2	20020822	WO 2002-US4431	20020213
WO 2002064091	A3	20030313		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-268591P P 20010213
OTHER SOURCE(S): MARPAT 137:190724

AB Metallopeptides are provided for use in treatment of **sexual** dysfunction in mammals. The metallopeptides are agonists for at least one of **melanocortin**-3 or **melanocortin**-4 receptors. The metallopeptides are conformationally fixed on complexation of a metal ion-binding portion thereof with a metal ion. Also provided are metallopeptides that are antagonists for at least one of **melanocortin**-3 or **melanocortin**-4 receptors.

L18 ANSWER 15 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:595493 HCAPLUS
DOCUMENT NUMBER: 137:145614
TITLE: Pharmaceutical compositions containing a peptide for treatment of **sexual** dysfunction
INVENTOR(S): **Blood, Christine H.; Shadiack, Annette M.; Bernstein, Joanna K.; Herbert, Guy H.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 606,501.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002107182	A1	20020808	US 2002-40547	20020104
US 6579968	B1	20030617	US 2000-606501	20000628

PRIORITY APPLN. INFO.: US 1999-142346P P 19990629
US 2000-194987P P 20000405
US 2000-606501 A2 20000628

AB Compns. and methods are provided for treatment of **sexual** dysfunction in mammals, including male **sexual** dysfunction, such as erectile dysfunction, and female **sexual** dysfunction. In one embodiment, a peptide-based compn. including the peptide sequence Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH (I) is administered. Methods of administration include injection, oral, nasal and mucosal administration. I was dissolved in a 50 mM citrate, pH approx. 6.0, at a

concn. of .825 mg per mL to obtain a nasal soln. Nasal administration of I at a concn. of 25 .mu.k/kg induced 100% penile erection in rats for 2 times in 30 min.

L18 ANSWER 16 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:529810 HCAPLUS
DOCUMENT NUMBER: 137:340097
TITLE: Structure-activity relationship and signal transduction of .gamma.-**MSH** peptides in GH3 cells: further evidence for a new **melanocortin** receptor
AUTHOR(S): Langouche, Lies; Pals, Katrien; Denef, Carl
CORPORATE SOURCE: Laboratory of Cell Pharmacology, K. U. Leuven, Medical School, Louvain, B-3000, Belg.
SOURCE: Peptides (New York, NY, United States) (2002), 23(6), 1077-1086
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The structure-activity relationship and signal transduction properties of the pro-opiomelanocortin (POMC)-derived .gamma.-**MSH** peptides in the GH3 cell line was compared with that described for the known **melanocortin** receptors (MCRs). Single alanine replacements showed that, unlike the classical MCRs, the His5-Phe6-Arg7-Trp8 sequence in .gamma.2-**MSH** is not a core sequence for activating the .gamma.-**MSH** receptor in GH3 cells, whereas Met3 is essential. .gamma.2-**MSH** increased binding of [35S]GTP.gamma.S to membrane prepns. of GH3 cells. Blockade of protein kinase A abolished the [Ca2+]i responses to .gamma.3-**MSH**, and low nanomolar doses of .gamma.3-**MSH** increased intracellular cAMP levels, which could be blocked by pertussis toxin (PTX). We conclude that the putative novel .gamma.-**MSH** receptor in GH3 cells is a GPCR, but with structure-activity and signal transduction features different from those of the classical MCRs.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 17 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:417177 HCAPLUS
DOCUMENT NUMBER: 137:135211
TITLE: Structure-Activity Relationships of the **Melanocortin** Tetrapeptide Ac-His-DPhe-Arg-Trp-NH2 at the Mouse **Melanocortin** Receptors: Part 2 Modifications at the Phe Position
AUTHOR(S): Holder, Jerry Ryan; Bauzo, Rayna M.; Xiang, Zhimin; Haskell-Luevano, Carrie
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610-0485, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(14), 3073-3081
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **melanocortin** pathway is an important participant in skin pigmentation, steroidogenesis, obesity, energy homeostasis and exocrine gland function. The centrally located **melanocortin**-3 and **melanocortin**-4 receptors (MC3R, MC4R) are involved in the metabolic and food intake aspects of energy homeostasis and are stimulated

by **melanocortin** agonists such as .alpha.-**melanocyte** stimulation hormone (.alpha.-**MSH**). The **melanocortin** agonists contain the putative message sequence "His-Phe-Arg-Trp," and it has been well-documented that inversion of chirality of the Phe to DPhe results in a dramatic increase in **melanocortin** receptor potency. Herein, the authors report a tetrapeptide library, based upon the template Ac-His-DPhe-Arg-Trp-NH2, consisting of 26 members that have been modified at the DPhe7 position (.alpha.-**MSH** numbering) and pharmacol. characterized for agonist and antagonist activity at the mouse **melanocortin** receptors MC1R, MC3R, MC4R, and MC5R. The most notable results of this study include the identification of the tetrapeptide Ac-His--(pI)DPhe-Arg-Trp-NH2 that is a full nanomolar agonist at the mMC1 and mMC5 receptors, a mMC3R partial agonist with potent antagonist activity (pA2 = 7.25, Ki = 56 nM) and, but unexpectedly, is a potent agonist at the mMC4R (EC50 = 25 nM). This ligand possesses novel **melanocortin** receptor pharmacol., as compared to previously reported peptides, and is potentially useful for in vivo studies to differentiate MC3R vs. MC4R physiol. roles in animal models, such as primates, where "knockout" animals are not viable options. The DNal(2') substitution for DPhe resulted in a mMC3R partial agonist with antagonist activity (pA2 = 6.5, Ki = 295 nM) and a mMC4R (pA2 = 7.8, Ki = 17 nM) antagonist possessing 60- and 425-fold decreased potency, resp., as compared with SHU9119 at these receptors. Examn. of this DNal(2')-contg. tetrapeptide at the F254S and F259S mutant mMC4Rs resulted in agonist activity of this mMC4R tetrapeptide antagonist, similar to that obsd. for the SHU9119 peptide, supporting the authors' previously proposed hypothesis that the Phe 254 and 259 transmembrane six receptor residues are important for differentiating **melanocortin** sequence-based MC4R antagonists vs. the agouti-related protein (AGRP) sequence-based antagonists.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:394477 HCAPLUS
DOCUMENT NUMBER: 137:103998
TITLE: Structure-Activity Relationships of the **Melanocortin** Tetrapeptide Ac-His-DPhe-Arg-Trp-NH2 at the Mouse **Melanocortin** Receptors. 1. Modifications at the His Position
AUTHOR(S): Holder, Jerry Ryan; Bauzo, Rayna M.; Xiang, Zhimin; Haskell-Luevano, Carrie
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(13), 2801-2810
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **melanocortin** pathway is an important participant in obesity and energy homeostasis. The centrally located **melanocortin**-3 and **melanocortin**-4 receptors (MC3R, MC4R) are involved in the metabolic and food intake aspects of energy homeostasis and are stimulated by **melanocortin** agonists such as .alpha.-**melanocyte** stimulation hormone (.alpha.-**MSH**). The **melanocortin** agonists contain the putative message sequence "His-Phe-Arg-Trp", and it has been well documented that inversion of chirality of the Phe to DPhe results in a dramatic increase in **melanocortin** receptor potency.

Search completed by David Schreiber 308-4292

Herein, the authors report a tetrapeptide library based on the template Ac-His-DPhe-Arg-Trp-NH2, consisting of 17 members that have been modified at the His6 position (.alpha.-**MSH** numbering) and pharmacol. characterized for agonist activity at the mouse **melanocortin** receptors MC1R, MC3R, MC4R, and MC5R. These studies provide further exptl. evidence that the His6 position can det. MC4R vs. MC3R agonist selectivity and that chem. nonreactive side chains may be substituted for the imidazole ring (generally needs to be side chain protected in synthetic schemes) in the design of MC4R-selective, small-mol., non-peptide agonists. Specifically, the tetrapeptide contg. the amino-2-naphthylcarboxylic acid (Anc) amino acid at the His position resulted in a potent agonist at the mMC4R (EC50 = 21 nM), was a weak mMC3R micromolar antagonist (pA2 = 5.6, Ki = 2.5 .mu.M), and possessed >4700-fold agonist selectivity for the MC4R vs. the MC3R. Substitution of the His6 amino acid in the tetrapeptide template by the Phe, Anc, 3-(2-thienyl)alanine (2Thi), and 3-(4-pyridinyl)alanine (4-Pal) resulted in equipotency or only up to a 7-fold decrease in potency, compared to the His6-contg. tetrapeptide at the mMC4R, demonstrating that these amino acid side chains may be substituted for the imidazole in the design of MC4R-selective non-peptide mols.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 19 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:220921 HCAPLUS
DOCUMENT NUMBER: 136:257757
TITLE: Method for treatment of insulin resistance in obesity and diabetes and for identifying compounds useful for reducing insulin resistance
INVENTOR(S): Brennan, Miles B.; Hochgeschwender, Ute
PATENT ASSIGNEE(S): Eleanor Roosevelt Institute, USA; Oklahoma Medical Research Foundation
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002023184	A1	20020321	WO 2001-US28720	20010913
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001092658	A5	20020326	AU 2001-92658	20010913
US 2002099014	A1	20020725	US 2001-953349	20010913
EP 1322954	A1	20030702	EP 2001-973036	20010913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-232292P P 20000913
WO 2001-US28720 W 20010913

AB Disclosed is a method to identify compds. useful for reducing insulin

resistance is a patient, and particularly a patient that has insulin resistance assocd. with obesity and/or type II diabetes. Also disclosed is a method of reducing insulin resistance in a patient by administering a compd. identified using the method of the invention, and particularly, by administering an antagonist of **melanocortin** stimulating hormone (**MSH**) biol. activity.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 20 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:924031 HCAPLUS
DOCUMENT NUMBER: 136:50668
TITLE: High throughput method for screening candidate compounds for biological activity
INVENTOR(S): Haizlip, Jill Elaine; Ignar, Diane Michele; Jayawickreme, Channa K.; King, Holly Kay; Liacos, James Arthur; Mills, Kirsten; Ruan, Jason J.; Sauls, Howard Ray, Jr.; Shaffer, Joel Edward
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096597	A2	20011220	WO 2001-US19033	20010613

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-211268P P 20000613
US 2001-294531P P 20010530

AB A method for high throughput screening of compds. ranging from drugs to receptors is described. The invention provides a novel assay method for screening candidate compds. for an ability to module the biol. activity of a target.

L18 ANSWER 21 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:651571 HCAPLUS
DOCUMENT NUMBER: 135:205579
TITLE: HP-3228 and related peptides to treat **sexual** dysfunction
INVENTOR(S): Girten, Beverly E.; Tuttle, Ronald R.
PATENT ASSIGNEE(S): Lion Bioscience A.-G., Germany
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 306,686.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6284735	B1	20010904	US 1999-356386	19990716
US 6127381	A	20001003	US 1999-301391	19990428
US 6608082	B1	20030819	US 1999-306686	19990506
WO 2001005401	A1	20010125	WO 2000-US19408	20000713

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6534503	B1	20030318	US 2000-615479	20000713

PRIORITY APPLN. INFO.:

US 1998-83368P	P	19980428
US 1999-301391	A1	19990428
US 1999-306686	A2	19990506
US 1999-356386	A	19990716
US 1999-364825	A	19990730
US 1999-401004	A	19990921

OTHER SOURCE(S): MARPAT 135:205579

AB Methods for treating erectile dysfunction in males and **sexual** dysfunction, such as **sexual** arousal disorder, in females. The methods involve administering an effective amt. of certain compds. such as HP-228 (Ac-Nle-Gln-His(D)Phe-Arg-(D)Trp-Gly-NH2).

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 22 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:428312 HCAPLUS

DOCUMENT NUMBER: 135:132543

TITLE: Characterization of **melanocortin** NDP-**MSH** agonist peptide fragments at the mouse central and peripheral **melanocortin** receptors

AUTHOR(S): Haskell-Luevano, Carrie; Holder, Jerry Ryan; Monck, Eileen K.; Bauzo, Rayna M.

CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610, USA

SOURCE: Journal of Medicinal Chemistry (2001), 44(13), 2247-2252
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The central **melanocortin** receptors, **melanocortin**-4 (MC4R) and **melanocortin**-3 (MC3R), are involved in the regulation of satiety and energy homeostasis. The MC4R in particular has become a pharmaceutical industry drug target due to its direct involvement in the regulation of food intake and its potential therapeutic application for the treatment of obesity-related diseases. The **melanocortin** receptors are stimulated by the native ligand, .alpha.-**MSH**. The potent and enzymically stable analog NDP-**MSH** (Ac-Ser-Tyr-Ser-Nle-Glu-His-DPhe-Arg-Trp-Gly-Lys-Pro-Val-NH2) is a lead peptide for the identification of **melanocortin** amino acids important for receptor mol. recognition and stimulation. The authors have

synthesized nine peptide fragments of NDP-**MSH**, deleting N- and C-terminal amino acids to det. the "minimally active" sequence of NDP-**MSH**. Addnl., five peptides were synthesized to study stereochem. inversion at the Phe 7 and Trp 9 positions in attempts to increase tetra- and tripeptide potencies. These peptide analogs were pharmacol. characterized at the mouse **melanocortin** MC1, MC3, MC4, and MC5 receptors. This study has identified the Ac-His-DPhe-Arg-Trp-NH2 tetrapeptide as possessing 10 nM agonist activity at the brain MC4R. The tripeptide Ac-DPhe-Arg-Trp-NH2 possessed micromolar agonist activities at the MC1R, MC4R, and MC5R but only slight stimulatory activity was obsd. at the MC3R (at up to 100 .mu.M concn.). This study has also examd. to importance of both N- and C-terminal NDP-**MSH** amino acids at the different **melanocortin** receptors, providing information for drug design and identification of putative ligand-receptor interactions.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 23 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:360169 HCAPLUS
DOCUMENT NUMBER: 134:362269
TITLE: Protein and cDNA sequences of human chordin-like homologs (CLH) and diagnostic and therapeutic uses thereof
INVENTOR(S): Toporoik, Amir; Biton, Sharon; Savitzky, Kinneret; **Bernstein, Jeanne**
PATENT ASSIGNEE(S): Compugen Ltd., Israel
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034796	A1	20010517	WO 2000-IL736	20001110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1230359	A1	20020814	EP 2000-973208	20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: IL 1999-132846 A 19991110
IL 1999-133767 A 19991228
WO 2000-IL736 W 20001110

AB The present invention provides protein and cDNA sequences of several splice variants of human chordin-like homologs (CLH) and a mouse chordin. The invention also provides expression vectors contg. DNA encoding the chordin-like homolog and host cells transformed with expression vectors for the recombinant prodn. of the chordin-like homolog. Northern blot anal. shows that CLH mRNA of 2.3kb is detected at significantly high levels in uterus, and also in colon, bladder, heart, stomach and prostate tissues. Expression of CLH mRNA was also found in different human cDNA

tissues, such as: testis, placenta, brain, bone marrow, ovary, fetal lung, fetal brain. Immunohistochem. staining is performed on different human microsections using the anti-LM antibodies found that CLH is expressed in different epithelial tissues and localized mainly in the secreting cells. In one embodiment, the invention relates to assays for detecting the chordin-like homolog in biol. samples. Also disclosed are methods for utilizing the chordin-like homolog in drug screening assays and in therapy directed against diseases assocd. with inappropriate CLH activity or levels.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 24 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:137478 HCAPLUS
DOCUMENT NUMBER: 134:188233
TITLE: **Melanocortin** metallopeptide constructs, combinatorial libraries, and applications
INVENTOR(S): Sharma, Shubh D.; Shi, Yi-Qun; Yang, Wei; Cai, Hui-Zhi
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001013112	A1	20010222	WO 2000-US16396	20000615
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1208377	A1	20020529	EP 2000-944681	20000615
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-148994P P 19990812
WO 2000-US16396 W 20000615
OTHER SOURCE(S): MARPAT 134:188233
AB Metallopeptides and metallopeptide combinatorial libraries specific for **melanocortin** receptors are provided, for use in biol., pharmaceutical and related applications. The metallopeptides and combinatorial libraries are made of peptides, peptidomimetics and peptide-like constructs, in which the peptide, peptidomimetic or construct is conformationally fixed on complexation of a metal ion-binding portion thereof with a metal ion.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 25 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:63828 HCAPLUS
DOCUMENT NUMBER: 134:116238
TITLE: **Melanocortin** receptor-3 ligands to treat **sexual** dysfunction

Kam 10/040,547

INVENTOR(S): Dines, Kevin C.; Gahman, Timothy C.; Girten, Beverly E.; Hitchin, Douglas L.; Holme, Kevin R.; Lang, Hengyuan; Slivka, Sandra R.; Watson-Straughan, Karen J.; Tuttle, Ronald R.; Pei, Yazhong
PATENT ASSIGNEE(S): Trega Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005401	A1	20010125	WO 2000-US19408	20000713
W:	AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6284735	B1	20010904	US 1999-356386	19990716

PRIORITY APPLN. INFO.:

US 1999-356386	A	19990716
US 1999-364825	A	19990730
US 1999-401004	A	19990921
US 1998-83368P	P	19980428
US 1999-301391	A1	19990428
US 1999-306686	A2	19990506

OTHER SOURCE(S): MARPAT 134:116238

AB Methods for treating **sexual** dysfunction, such as erectile dysfunction or **sexual** arousal disorder, with a compd. having the generic formula X1-X2-D-Phe-Arg-D-Trp-X3 [X1 = R1R2NCHR3CY1Y2, Ac, H, or absent, where R1 = R2, COPh, CO2Bu-t, CO2CH2Ph, CHCO-(polyethylene glycol) or A which is N,O-(un)substituted 3-amino-4,5,6-trihydroxytetrahydro-2-pyranyl; R2 = H, Ac, Et, PhCH2; R3 = alkyl, cycloalkyl; Y1, Y2 = H or together form carbonyl or thiocarbonyl; X2 = NR1CHR4CY1Y2-His, His, Ac, or H, where R4 = (CH2)mCONH2, (CH2)mCONHR1, or (CH2)CONHA (m = 1-3); X3 = NR1CHR6(CH2)nCY1Y2R5 or R5, where R5 = OH, OR3, NH2, SH, NHMe, NHCH2PH, or A; R6 = H or R3, n = 0-3]. A particularly useful compd. is HP-228, which has the formula Ac-Nle-Gln-His-D-Phe-Arg-D-Trp-Gly-NH2. The invention also provides methods for selecting **melanocortin** receptor-3 ligands by detg. whether a compd. modulates the activity of MC-3 as an agonist or antagonist. These methods can be used to screen compd. libraries, including benzimidazoles, for ligands to treat MC-3-assocd. conditions. Such conditions include **sexual** dysfunction, including erectile dysfunction and **sexual** arousal disorder (data given).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 26 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:12284 HCAPLUS
DOCUMENT NUMBER: 134:76409
TITLE: Compositions and methods for treatment of **sexual** dysfunction

Search completed by David Schreiber 308-4292

INVENTOR(S): **Blood, Christine H.; Shadiack, Annette M.; Bernstein, Joanna K.; Herbert, Guy W.**
PATENT ASSIGNEE(S): Palatin Technologies Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000224	A1	20010104	WO 2000-US18217	20000629
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6579968	B1	20030617	US 2000-606501	20000628
BR 2000012200	A	20020326	BR 2000-12200	20000629
EP 1196184	A1	20020417	EP 2000-950283	20000629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003503357	T2	20030128	JP 2001-505933	20000629

PRIORITY APPLN. INFO.:
US 1999-142346P P 19990629
US 2000-194987P P 20000405
US 2000-606501 A 20000628
WO 2000-US18217 W 20000629

AB Compns. and methods are provided for the treatment of **sexual** dysfunctions in mammals, such as erectile dysfunction and female **sexual** dysfunction. In one embodiment, a peptide-based compn. including the peptide sequence Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH is administered. Methods of administration include injection, oral, nasal and mucosal administration.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 27 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:757160 HCAPLUS
DOCUMENT NUMBER: 134:640
TITLE: Molecular determinants of ligand binding to the human **melanocortin**-4 receptor
AUTHOR(S): Yang, Ying-kui; Fong, Tung M.; Dickinson, Chris J.; Mao, Cheri; Li, Ji-Yao; Tota, Michael R.; Mosley, Ralph; Van der Ploeg, Lex H. T.; Gantz, Ira
CORPORATE SOURCE: Departments of General Surgery and Pediatrics, University of Michigan Medical School, Ann Arbor, MI, 48109, USA
SOURCE: Biochemistry (2000), 39(48), 14900-14911
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To elucidate the mol. basis for the interaction of ligands with the human

melanocortin-4 receptor (hMC4R), agonist structure-activity studies and receptor point mutagenesis were performed. Structure-activity studies of [Nle4,D-Phe7]-.alpha.-**MSH** (NDP-**MSH**) identified D-Phe7-Arg8-Trp9 as the minimal NDP-**MSH** fragment that possesses full agonist efficacy at the hMC4R. In an effort to identify receptor residues that might interact with amino acids in this tripeptide sequence 24 hMC4R transmembrane (TM) residues were mutated. Mutation of TM3 residues D122 and D126 and TM6 residues F261 and H264 decreased the binding affinity of NDP-**MSH** 5-fold or greater, thereby identifying these receptor residues as sites potentially involved in the sought after ligand-receptor interactions. By examn. of the binding affinities and potencies of substituted NDP-**MSH** peptides at receptor mutants, evidence was found that core **melanocortin** peptide residue Arg 8 interacts at a mol. level with hMC4R TM3 residue D122. TM3 mutations were also obsd. to decrease the binding of hMC4R antagonists. Notably, mutation of TM3 residue D126 to alanine decreased the binding affinity of AGRP (87-132), a C-terminal deriv. of the endogenous **melanocortin** antagonist, 8-fold, and simultaneous mutations D122A/D126A completely abolished AGRP (87-132) binding. In addn., mutation of TM3 residue D122 or D126 decreased the binding affinity of hMC4R antagonist SHU 9119. These results provide further insight into the mol. determinants of hMC4R ligand binding.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 28 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:720145 HCAPLUS
DOCUMENT NUMBER: 133:329701
TITLE: David and Goliath - the slingshot that started the neuropeptide revolution
AUTHOR(S): Strand, F. L.
CORPORATE SOURCE: Department of Biology and Center for Neural Science, New York University, New York, NY, 10003, USA
SOURCE: European Journal of Pharmacology (2000), 405(1-3), 3-12
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 49 refs. This review in honor of David de Wied summarizes the work done in my lab. that first indicated that adrenocorticotropic hormone (ACTH) has a direct effect on the neuromuscular system. Cold stress or ACTH and its related peptides .alpha.-**MSH** and .beta.-lipotropin improve the electromech. characteristics of adrenalectomized and hypophysectomized rats. ACTH-(1-39) accelerates the return of motor and sensory function and improves the morphol. characteristics of the motor endplate after peripheral nerve crush. The non-corticotropic fragments ACTH-(4-10), .alpha.-**MSH**, the ACTH-(4-9) analog Organon 2766 (Org 2766) or the ACTH-(4-10) analog Biomeasure 22015 (BIM 22015) improve electrophysiol. and morphol. parameters of the regenerating neuromuscular system. ACTH-(4-10) immunoreactivity, present in ventral horn motor neurons in low levels, is decreased ipsilaterally following ipsilateral nerve crush but increases both ipsilaterally and contralaterally if injured animals are treated with ACTH-(4-10) indicating a neuroprotective action. Similarly, Org 2766 appears to have a protective action in the brain following nigrostriatal lesions. In developmental studies, perinatal exposure to ACTH peptides improves the structure of the neuromuscular junction, accelerates the maturation of electromech. properties and enhances nerve-muscle

integration and nerve regeneration. Perinatal exposure to these peptides decreases adult male **sexual** behavior, a change correlated with increased serotonergic input within the medial preoptic area. Similar changes occur in female rats and appear to be long-lasting. In tissue culture studies, both Org 2766 and BIM 22015 promote neurite outgrowth in the absence of nerve growth factor, indicating a neurotrophic role for these peptides.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 29 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:591208 HCAPLUS
DOCUMENT NUMBER: 133:261657
TITLE: Structure-activity studies of .alpha.-melanotropin fragments on cAMP production in striatal slices
AUTHOR(S): Cecilia Cremer, M.; Silvina Sanchez, M.; Ester Celis, M.
CORPORATE SOURCE: Facultad de Ciencias Quimicas, Departamento de Farmacologia, Laboratorio de Fisiologia, Universidad Nacional de Cordoba, Cordoba, Argent.
SOURCE: Peptides (New York) (2000), 21(6), 803-806
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors characterized the active site in the .alpha.-melanotropin hormone (.alpha.-**MSH**) sequence responsible for the enhancement of cAMP prodn. in incubated striatal slices by using different .alpha.-**MSH** fragments. The authors also analyzed the effects of the co-incubation of the SCH23390, a dopaminergic D1 antagonist, with the **MSH** fragments, to study the involvement of the D1 receptor on this induction. A rise was obsd. in the levels of cAMP after addn. of the 6 .mu.M fragments **MSH**(1-10), and 0.6 and 6 .mu.M **MSH** (5-13); however, the values were lower than those induced by 6 .mu.M .alpha.-**MSH**. On the contrary, the addn. of **MSH**(9-13), **MSH**(7-11), or **MSH**(6-9) did not affect the cAMP content. The presence of 10 .mu.M SCH23390 blocked the effect of the fragments on cAMP prodn. The authors conclude that the biol. activity of .alpha.-**MSH**, as obsd. through the levels of cAMP, declines when the length of its polypeptide chain is shortened, and that the presence of glutamic acid in the mol., as well as the core sequence, are of importance for fragments' activity.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 30 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:422404 HCAPLUS
DOCUMENT NUMBER: 133:99692
TITLE: Analogs of lactam derivatives of .alpha.-melanotropin with basic and acidic residues
AUTHOR(S): Bednarek, Maria A.; MacNeil, Tanya; Kalyani, Rubana N.; Tang, Rui; Van der Ploeg, Lex H. T.; Weinberg, David H.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Biochemical and Biophysical Research Communications (2000), 272(1), 23-28
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A role of the arom. and of the basic residues of the potent agonist (MTII) and antagonist (SHU 9119) at the human **melanocortin** receptors 4 in the formation and stabilization of ligand-receptor complexes was examd. Analogs of MTII and SHU 9119 with glutamic acid replacing one amino acid at a time were synthesized and tested for their ability to bind to and activate human **melanocortin** receptors 3, 4, and 5. Replacement of Phe (Nal) or Trp with Glu resulted in analogs of MTII and SHU 9119 which were practically inactive at the receptors studied. The rather large (and unexpected) tolerance toward the presence of Glu in the position of His or Arg of MTII and SHU 9119 clearly suggested that in the ligand receptor complexes these basic residues are not in contact with the receptors but probably face the extracellular environment. This identified the arom. residues of MTII and SHU 9119 as the primary structural features detg. interactions of the agonist/antagonist with hMCR3-5. (c) 2000 Academic Press.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 31 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:401591 HCAPLUS
DOCUMENT NUMBER: 133:38707
TITLE: Composition and method for regulation of body weight and associated conditions by administering proopiomelanocortin peptides or analogs thereof
INVENTOR(S): Brennan, Miles B.; Hochgeschwender, Ute
PATENT ASSIGNEE(S): Eleanor Roosevelt Institute, USA; Oklahoma Medical Research Foundation
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000033658	A1	20000615	WO 1999-US29337	19991209
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6603058	B1	20030805	US 1999-374827	19990812
EP 1137340	A1	20011004	EP 1999-965208	19991209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2003144174	A1	20030731	US 1999-458579	19991209

PRIORITY APPLN. INFO.:
US 1998-111581P P 19981209
US 1999-146299P P 19990729
US 1999-146300P P 19990729
US 1999-146301P P 19990729
US 1999-146302P P 19990729
US 1999-146303P P 19990729

Search completed by David Schreiber 308-4292

	US 1999-146304P	P	19990729
	US 1999-146305P	P	19990729
	US 1999-146306P	P	19990729
	US 1999-374827	A	19990812
	WO 1999-US29337	W	19991209

OTHER SOURCE(S): MARPAT 133:38707

AB Described are methods and compns. for regulating body wt. and/or regulating the rate of wt. gain or loss, and particularly, for treating or preventing obesity. Specifically, methods of administering varying levels of circulating proopiomelanocortin peptides or analogs thereof to an animal, alone or in combination with leptin or other body wt. regulating agents are disclosed. Methods and compns. for treating a variety of disorders assocd. with or caused by undesirable body wt. are also described. Also described are methods for identifying compds. useful for regulation of body wt. and assocd. conditions. In particular, methods are disclosed for identification of compds. that preferentially bind to and/or activate peripheral **melanocortin** receptors and which minimize binding and/or activation of central **melanocortin** receptors. Also described is a genetically modified non-human animal model for studying the peripheral and central pathways of energy homeostasis. Also disclosed are methods of identifying compds. for regulating such pathways and a POMC mutant mouse. The compns. of the invention include food and pharmaceutical compns.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 32 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:224777 HCAPLUS

DOCUMENT NUMBER: 133:189527

TITLE: Molecular Cloning of Proopiomelanocortin cDNA from an Elasmobranch, the Stingray, Dasyatis akajei

AUTHOR(S): Amemiya, Yutaka; Takahashi, Akiyoshi; Suzuki, Nobuo; Sasayama, Yuichi; Kawauchi, Hiroshi

CORPORATE SOURCE: Laboratory of Molecular Endocrinology, Kitasato University, Sanriku, Iwate, 022-0101, Japan

SOURCE: General and Comparative Endocrinology (2000), 118(1), 105-112
CODEN: GCENA5; ISSN: 0016-6480

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recently, we have characterized a new **MSH** (named .delta.-**MSH**) which joins the group of MSHs (.alpha., .beta., .gamma.) in dogfish proopiomelanocortin (POMC). The present study has confirmed the presence of .delta.-**MSH** in POMC of another member of the elasmobranchian order, the stingray, Dasyatis akajei, by cDNA cloning from pituitary mRNAs. Overlapping partial cDNA clones corresponding to stingray POMC were amplified by PCR from single-strand cDNA prepd. from pituitary poly (A)+ RNA. Excluding the poly A tail, stingray POMC cDNA consists of 1077 base pairs (bp). It contains a 912-bp open reading frame encoding a signal peptide of 24 amino acids (aa) and a POMC of 280 aa. .gamma.-**MSH**, .alpha.-**MSH**, ACTH, .delta.-**MSH**, .beta.-**MSH**, and .beta.-endorphin are located at POMC (50-61), (115-127), (115-153), (182-193), (226-242), and (245-280), resp. The stingray POMC is smaller than that of the dogfish POMC (294 aa) mainly due to the absence of a sequence of 11 consecutive aa between .delta.-**MSH** and .beta.-**MSH**. .delta.-**MSH** has been found only in the elasmobranchs and, therefore, .delta.-**MSH** might have evolved after the divergence of chondrichthians from the

ancestral vertebrate lineage and before divergence of sharks and rays.
(c) 2000 Academic Press.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 33 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:84853 HCAPLUS
DOCUMENT NUMBER: 132:117960
TITLE: Compounds containing amino acid sequence HFRW for use in the treatment of inflammation
INVENTOR(S): Perretti, Mauro; Getting, Stephen; Flower, Roderick
PATENT ASSIGNEE(S): William Harvey Research Limited, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005263	A2	20000203	WO 1999-GB2392	19990722
WO 2000005263	A3	20000504		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9950560	A1	20000214	AU 1999-50560	19990722

PRIORITY APPLN. INFO.: GB 1998-16234 A 19980724
WO 1999-GB2392 W 19990722

AB Use of a compd. comprising an amino acid sequence HFRW in the manuf. of a medicament for inhibition of neutrophil chemoattractant prodn., inhibition of polymorphonuclear cell (PMN) accumulation, or redn./treatment of inflammatory response/disease, and/or in the manuf. of an agonist of **melanocortin** receptor type 3 (MC3-R); wherein the compd. is not adrenocorticotropic hormone (ACTH)1-39 or a fragment thereof which activates the prodn. of glucocorticoids. Preferably the compd. is a polypeptide comprising the sequence MEHFRWG. Preferably the compd. is a fragment of ACTH (not one that activates prodn. of glucocorticoids), .beta.-**melanocortin**-stimulating hormone or a fragment thereof, or MT-II or a fragment thereof. The inflammatory response/disease being treated is gout, gouty arthritis, rheumatoid arthritis, asthma, reperfusion injury or damage, stroke, myocardial infarction, septic shock, or a skin disorder.

L18 ANSWER 34 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:84580 HCAPLUS
DOCUMENT NUMBER: 132:132355
TITLE: Dermatological compositions for the treatment of scars
INVENTOR(S): Ferguson, Mark William James; Chettibi, Salah
PATENT ASSIGNEE(S): Smith & Nephew Plc, UK
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004873	A1	20000203	WO 1999-GB2388	19990722
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9950557	A1	20000214	AU 1999-50557	19990722

PRIORITY APPLN. INFO.: GB 1998-15822 A 19980722
GB 1998-17143 A 19980806
WO 1999-GB2388 W 19990722

AB A compn. for the treatment of scars and chronic wounds or chronic scars, comprises .alpha.-**MSH** or its derivs. A soln. contg. .alpha.-**MSH** (1 .mu.g/mL) and 0.1 % bovine serum albumin in PBS was intradermally injected to on exptl. drawn wounds on the back of rats. The injections were repeated once a day for 5 days and wounds were harvested for histol. anal., which showed a marked improvement in wound repair by observing collagen fibers.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 35 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:14830 HCAPLUS
DOCUMENT NUMBER: 132:178208
TITLE: Occurrence of four MSHs in dogfish POMC and their immunomodulating effects
AUTHOR(S): Takahashi, Akiyoshi; Amemiya, Yutaka; Sakai, Masahiro; Yasuda, Akikazu; Suzuki, Nobuo; Sasayama, Yuichi; Kawauchi, Hiroshi
CORPORATE SOURCE: Laboratory of Molecular Endocrinology, School of Fisheries Sciences, Kitasato University, Iwate, 022-0101, Japan
SOURCE: Annals of the New York Academy of Sciences (1999), 885(Cutaneous Neuroimmunomodulation), 459-463
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB POMC cDNA prepd. from dogfish (Squalus acanthias) pituitary had an open reading frame that encodes a 320 amino acid sequence including a signal peptide of 26 amino acids. The dogfish POMC includes .gamma.-**MSH**, ACTH, .alpha.-**MSH**, .beta.-**MSH**, and .beta.-endorphin at positions 50-61, 115,-153, 115-127, 239-256, and 259-294, resp. In addn. to these classic peptides, a newly discovered **MSH**, which we have termed .delta.-**MSH**, is present in dogfish POMC at position 184-195. **MSH** isoforms enhance the activities of carp phagocytes.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Search completed by David Schreiber 308-4292

L18 ANSWER 36 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:617631 HCAPLUS
TITLE: Conformationally constrained metallopeptide template for **melanocortin**-1 receptor.
AUTHOR(S): Shi, Y.; Cai, Hui-Zhi; Yang, W. H.; **Blood, C.**; **Shadiack, A.**; Sharma, S.
CORPORATE SOURCE: 175 May Street, Palatin Technologies Inc., Edison, NJ, 08837, USA
SOURCE: Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (1999), MEDI-257. American Chemical Society: Washington, D. C.
CODEN: 67ZJA5
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB We are developing highly rigid and structurally well defined scaffolds for drug design by complexing a metal-ion to a pre-designed linear peptide.These scaffolds are functionally derivatized to induce affinity and specificity for a biol. receptor.Using the His-Phe-Arg-Trp message sequence of a-melanotropin we have developed a series of rhenium-complexed metallo-peptides and investigated these for melanotropic activity on **melanocortin** receptor-1 and 4 (MCR-1 and MCR-4).One of these metallopeptides (A) was highly specific for MCR-1 (IC.ident.1 mM).In cAMP accumulation assay it was a full agonist.The rigid structure of this metallopeptide representing a highly constrained configuration of the melanotropin message sequence, therefore, may define the pharmacophore for MCR-1.

L18 ANSWER 37 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:396488 HCAPLUS
DOCUMENT NUMBER: 131:194460
TITLE: Identification of prototype peptidomimetic agonists at the human **melanocortin** receptors, MC1R and MC4R
AUTHOR(S): Haskell-Luevano, Carrie; Sawyer, Tomi K.; Hadley, Mac E.; Hruby, Victor J.; Gantz, Ira
CORPORATE SOURCE: University of Michigan Medical Center, Ann Arbor, MI, 48109, USA
SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of the American Peptide Symposium, 15th, Nashville, June 14-19, 1997 (1999), Meeting Date 1997, 198-199. Editor(s): Tam, James P.; Kaumaya, Pravin T. P. Kluwer: Dordrecht, Neth.
CODEN: 67UCAR
DOCUMENT TYPE: Conference
LANGUAGE: Englisn
AB The goal of this study was to examine stereochem. modified tripeptides and tetrapeptides on the human **melanocortin** receptors to det. selectivity, functional properties (i.e., agonism), and to correlate with recent frog skin **melanocortin** studies. The tripeptides examd. in this study were only able to generate dose-response competitive binding curves at the hMC4R. Ac-DPhe-Arg-Trp-NH2 resulted in a 1.8-fold decreased potency compared with Ac-His-DPhe-Arg-Trp-NH2. Of particular note, however, is that Ac-His-DPhe-Arg-Trp-NH2 was able to generate the max. intracellular cAMP accumulation obsd. for NDP-**MSH**, but the tripeptide Ac-DPhe-Arg-Trp-NH2 resulted in only 40 % generation of maximal cAMP at 10 .mu.M concn. Ac-DPhe-Arg-DTrp-NH2 resulted in a 9 .mu.M binding affinity but was only able to generate 50% maximal cAMP accumulation at 10 .mu.M concn.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 38 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:322184 HCAPLUS
DOCUMENT NUMBER: 131:142216
TITLE: A newly characterized melanotropin in proopiomelanocortin in pituitaries of an elasmobranch, Squalus acanthias
AUTHOR(S): Amemiya, Yutaka; Takahashi, Akiyoshi; Suzuki, Nobuo; Sasayama, Yuichi; Kawauchi, Hiroshi
CORPORATE SOURCE: Laboratory of Molecular Endocrinology, School of Fisheries Sciences, Kitasato University, Sanriku, 022-0101, Japan
SOURCE: General and Comparative Endocrinology (1999), 114(3), 387-395
CODEN: GCENA5; ISSN: 0016-6480
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Proopiomelanocortin (POMC) is a precursor for ACTH, .ltoreq.3 mol. types of **MSH**, and .beta.-endorphin. This protein is thought to have evolved by duplication of **MSH** genomic segments. Here we report that the POMC in the dogfish, an elasmobranch, contains a 4th type of **MSH** in addn. to classical .alpha.-, .beta.-, and .gamma.-**MSH**. POMC cDNA was amplified by PCR from double-strand cDNA prepd. from dogfish pituitary and ligated into .lambda.ZAP II. The POMC cDNA is composed of 1315 bp without a poly(A) tail. Northern blot anal. detected a 1.4-kb signal of dogfish POMC mRNA. An open reading frame of the POMC cDNA encodes 320 amino acids, including a signal peptide of 26 amino acids. The dogfish POMC includes .gamma.-**MSH**, ACTH, .alpha.-**MSH**, .beta.-**MSH**, and .beta.-endorphin at positions 50-61, 115-153, 115-127, 239-256, and 259-294, resp. In addn. to these classical peptides, a newly discovered **MSH**, which we have termed .delta.-**MSH**, is present in dogfish POMC at position (184-195). The 4 dogfish MSHs can be sepd. into 2 groups based on their sequence identities: 1 pair consists of .alpha.-**MSH** and .gamma.-**MSH**, and the other consists of .beta.-**MSH** and .delta.-**MSH**, suggesting that .gamma.-**MSH** and .delta.-**MSH** may have been duplicated evolutionarily from .alpha.-**MSH** and .beta.-**MSH**, resp. .gamma.-**MSH** might first have appeared in early gnathostomes because it is absent in the most primitive vertebrate group, the agnathans. .delta.-**MSH**, which at this time is found only in chondrichthians, might have appeared after the divergence of chondrichthians from a lineage leading to osteichthyans and tetrapods. (c) 1999 Academic Press.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 39 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:380625 HCAPLUS
DOCUMENT NUMBER: 129:117941
TITLE: Selective properties of C- and N-terminals and core residues of the **melanocyte**-stimulating hormone on binding to the human **melanocortin** receptor subtypes
AUTHOR(S): Schioth, Helgi B.; Mutulis, Felikss; Muceniece, Ruta; Prusis, Peteris; Wikberg, Jarl E. S.
CORPORATE SOURCE: Department of Pharmaceutical Pharmacology, omedical Center, Uppsala University, Uppsala, S-751 24, Swed.

Search completed by David Schreiber 308-4292

SOURCE: European Journal of Pharmacology (1998), 349(2/3), 359-366
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We synthesized nine analogs of [Nle4,D-Phe7].alpha.-**MSH** (NDP) where (1) the N- or C-terminals were deleted or exchanged by those of .beta.- or .gamma.-**MSH** and (2) the core residues His6, Phe7, Arg8 and Trp9 were individually substituted by Glu6, .beta.-(2-naphthyl)-D-alanine (D-Nal7), Lys8 and His9, resp. We tested these analogs in ligand binding assays with cells transiently expressing the human **melanocortin** MC1, MC3, MC4 and MC5 receptors. The results show that the N-terminal segment (Ser1-Tyr2-Ser3) of NDP was not important for binding to **melanocortin** MC1 and MC4 receptors whereas it affects binding to **melanocortin** MC3 and MC5 receptors. The C-terminal segment (Gly10-Lys11-Pro12-Val13) of NDP was clearly important for binding to all the four **melanocortin** receptor subtypes. The data indicate that the low affinity of .gamma.-**MSH** for the **melanocortin** MC4 receptor is due to its C-terminal (Asp10-Arg11-Phe12). Substitution of D-Phe7 by D-Nal7 increased the affinity for the **melanocortin** MC4 receptor but not for the other **melanocortin** receptor subtypes. The other core residue substitutions lowered the affinity in a differentiated manner for each of the **melanocortin** receptors. These results are valuable for the mol. modeling and design of selective drugs for the **melanocortin** receptors.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 40 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:329283 HCAPLUS
DOCUMENT NUMBER: 129:76640

TITLE: Molecular pharmacology of neural **melanocortin** receptors

AUTHOR(S): Adan, R. A. H.; Oosterom, J.; Toonen, R. F. G.; Van Der Kraan, M.; Burbach, J. P. H.; Gispen, W. H.
CORPORATE SOURCE: Department of Medical Pharmacology, Rudolf Magnus Institute for Neurosciences, Utrecht University, Utrecht, 3508, Neth.

SOURCE: Receptors and Channels (1997), 5(3-4), 215-223
CODEN: RCHAE4; ISSN: 1060-6823
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cloning of **melanocortin** receptors opened new avenues to identify selective ligands for this receptor family. .gamma.-**MSH** was characterized as a **melanocortin**-3 receptor selective agonist. [D-Arg8]ACTH-(4-10) and [Pro8.10,Gly9]ACTH-(4-10) were characterized as **melanocortin**-4 receptor antagonists. The application of these ligands in vivo revealed that **melanocortin** -4 receptors mediate **melanocortin**-induced grooming behavior in the rat. Since researchers still lack potent and selective **melanocortin** receptor ligands, the authors performed homol. modeling and site directed mutagenesis of the **melanocortin**-4 receptor, to understand how **melanocortins** bind **melanocortin** receptors. A histidine at position 260 in the **melanocortin**-4 receptor is important for normal receptor function. However this residue is not forming a salt bridge with a glutamate at

position 92 to keep the receptor in an inactive conformation, nor with the glutamate in the **melanocortin** peptides as had been suggested before.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 41 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:436011 HCAPLUS
DOCUMENT NUMBER: 127:76156
TITLE: Discovery of Prototype Peptidomimetic Agonists at the Human **Melanocortin** Receptors MC1R and MC4R
AUTHOR(S): Haskell-Luevano, Carrie; Hendrata, Siska; North, Cheryl; Sawyer, Tomi K.; Hadley, Mac E.; Hruby, Victor J.; Dickinson, Chris; Gantz, Ira
CORPORATE SOURCE: Departments of Internal Medicine Pediatrics and Surgery, University of Michigan Medical Center, Ann Arbor, MI, 48109, USA
SOURCE: Journal of Medicinal Chemistry (1997), 40(14), 2133-2139
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB [Nle4,DPhe7]-.alpha.-**MSH** (NDP-**MSH**), a highly potent analog of .alpha.-**MSH** , possesses nanomolar efficacies at all the **melanocortin** receptor subtypes except the MC2R. Evaluation of the **melanocortin** "message" sequence of [Nle4,DPhe7]-.alpha.-**MSH** was performed on the human **melanocortin** receptor subtypes designated hMC1, hMC3R, hMC4R, and hMC5R. Tetrapeptides and tripeptides were stereochem. modified to explore topochem. preferences at these receptors and to identify lead peptides possessing agonist activity and subtype selectivity. Four peptides were discovered to only bind to the hMC1 and hMC4 receptor subtypes. The tetrapeptide Ac-His-DPhe-Arg-Trp-NH2 possessed 0.6 .mu.M binding affinity at the hMC1R, 1.2 .mu.M binding affinity at the hMC4R, and agonist activity at both receptors. The tripeptides Ac-DPhe-Arg-Trp-NH2 and Ac-DPhe-Arg-DTrp-NH2 possessed 2.0 and 9.1 .mu.M binding affinities, resp., only at the hMC4R, and both compds. effected agonist activity. The tetrapeptide Ac-His-Phe-Arg-DTrp-NH2 possessed 6.3 .mu.M affinity and full agonist activity at the hMC1R, while only binding 7% at the hMC3R, 36% at the hMC4R, and 11% at the hMC5R at a maximal concn. of 10 .mu.M. These data demonstrate that the His-Phe-Arg-Trp message sequence of the **melanocortin** peptides does not bind and stimulate each **melanocortin** receptor in a similar fashion, as previously hypothesized. Addnl., this study identified the simplest structural agonists for the hMC1R and hMC4R receptors reported to date.

L18 ANSWER 42 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:140278 HCAPLUS
DOCUMENT NUMBER: 126:144560
TITLE: Preparation of conjugates of peptide alpha **MSH** with a fatty acid as antiallergy and antiinflammatory agents
INVENTOR(S): Dussourd d'Hinterland, Lucien; Pinel, Anne-Marie
PATENT ASSIGNEE(S): Institut Europeen De Biologie Cellulaire, Fr.; Dussourd d'Hinterland, Lucien; Pinel, Anne-Marie
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

Search completed by David Schreiber 308-4292

LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9641815	A2	19961227	WO 1996-FR890	19960612
WO 9641815	A3	19970130		
W: AU, CA, IL, JP, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2735131	A1	19961213	FR 1995-6909	19950612
FR 2735131	B1	19970822		
AU 9663094	A1	19970109	AU 1996-63094	19960612
EP 837881	A2	19980429	EP 1996-922103	19960612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11507661	T2	19990706	JP 1996-502708	19960612

PRIORITY APPLN. INFO.: FR 1995-6909 19950612
WO 1996-FR890 19960612

OTHER SOURCE(S): MARPAT 126:144560

AB A peptide conjugate comprising a peptide sequence that includes at least one sequence of four .alpha.**MSH**-derived amino acids optionally in a natural form, said sequence being chem. or phys. conjugated with acids selected from either dicarboxylic acids of general formula HOOC-R1-COOH or R2-CH=CH-COOH wherein R1 is a straight or branched alkylene radical having at least 3 and preferably 3-10 carbon atoms, and being optionally substituted, in particular by one or more amino or hydroxy groups; or .alpha.-monounsatd. fatty acids with a cis or preferably trans configuration, wherein R2 is straight or branched alkyl radical having at least 6 and preferably 6-10 carbon atoms, and being substituted by an amino, hydroxy or oxo group. Thus, adipoyl-MeNle-Glu-His-para-fluoro-Phe-Arg-Trp-Gly-NH2 was prepd. and tested as antiallergy and antiinflammatory agents.

L18 ANSWER 43 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:64422 HCAPLUS
DOCUMENT NUMBER: 126:166560
TITLE: Binding of cyclic and linear **MSH** core peptides to the **melanocortin** receptor subtypes
AUTHOR(S): Schioeth, Helgi B.; Muceniece, Ruta; Larsson, Monika; Mutulis, Felikss; Szardenings, Michael; Prusis, Peteris; Lindeberg, Gunnar; Wikberg, Jarl E. S.
CORPORATE SOURCE: Department of Pharmaceutical Pharmacology, Biomedical Center, Uppsala University, Box 591, 751 24, Uppsala, Swed.
SOURCE: European Journal of Pharmacology (1997), 319(2/3), 369-373
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors report the binding of 5-, 6- and 7-amino-acid-long linear and cyclic core peptides of **MSH** to cells transiently expressing the human **melanocortin** MC1, MC3, MC4 and MC5 receptors. The results show that, in contrast to the natural peptides, the core peptides did not differentiate between the **melanocortin** MC3 and MC4 receptors. All tested cyclic peptides had much lower affinities than their corresponding linear homologs. Interestingly, the relative loss of

binding due to the cyclization did not change as the ring size decreased. Therefore, decreasing the ring size does not seem to force the peptide into a more unfavorable conformation.

L18 ANSWER 44 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:43873 HCAPLUS
DOCUMENT NUMBER: 126:127046
TITLE: Structure-activity analysis for the effects of .gamma.-**MSH**/ACTH-like peptides on cerebral hemodynamics in rats
AUTHOR(S): Van Bergen, Patricia; Van Der Vaart, Jan G. M.; Kasbergen, Carina M.; Versteeg, Dirk H. G.; De Wildt, Dick J.
CORPORATE SOURCE: Department of Medical Pharmacology, Rudolf Magnus Institute for Neurosciences, Utrecht University, Universiteitsweg 100, CG Utrecht, 3584, Neth.
SOURCE: European Journal of Pharmacology (1996), 318(2/3), 357-368
CODEN: EJPHAZ; ISSN: 0014 2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a previous structure-activity anal. the authors have shown that the .gamma.-**melanocyte**-stimulating hormones (.gamma.-MSHs) and structurally related adrenocorticotropic hormone (ACTH) fragments share an amino-acid sequence which is determinant for the effects of these peptides on peripheral hemodynamics, viz. a pressor and a tachycardiac response, in conscious rats. The authors now investigated whether these structural features are also important for the effects of these peptides on cerebral hemodynamics in urethane-anesthetized rats. After intracarotid and i.v. administration, the 'mother' peptides, Lys-.gamma.2-**MSH** and .gamma.2-**MSH**, and, with a 10-fold lower potency, ACTH-(4-10), caused a dose-dependent pressor and tachycardiac response, as well as an increase in extra- and intracranial blood flow and microcirculatory cerebrocortical blood flow. Removal of C-terminal amino acids resulted in .gamma.-**MSH**-fragments which were devoid of effects on peripheral and central hemodynamics. Fragments of .gamma.2-**MSH** which were shortened at the N-terminal side (.gamma.-**MSH**-(4-12) and .gamma.-**MSH**-(5-12)) were less potent than .gamma.2-**MSH**, but had an intrinsic activity similar to that of .gamma.2-**MSH** with respect to the pressor and tachycardiac effect. However, the potency and intrinsic activity of these shortened fragments on intracerebral hemodynamic parameters were the same as those of .gamma.2-**MSH**. This suggests that different mechanisms (e.g., site of action and/or **melanocortin** receptor subtype) are involved in the cerebral hemodynamic effects of the **melanocortins** and in their peripheral hemodynamic effects. Surprisingly, removal of an addnl. residue, His5, resulting in the fragment .gamma.-**MSH**-(6-12), led to full restoration of potency with respect to extracranial blood flow, blood pressure and heart rate. Neither the structurally related analog, [Nle4,D-Phe7].alpha.-**MSH** (NDP-**MSH**), nor ACTH-(1-24) was able to induce a pressor effect or cerebral hemodynamic effects. In contrast, both compds. had a depressor effect. It is concluded that the C-terminal amino acids in the structure of .gamma.-**MSH**/ACTH-like peptides are essential for efficacy for the central hemodynamic effects, i.e., the increase in intracerebral (microcirculatory) blood flow. However, in contrast to what holds for the peripheral hemodynamic features, the N-terminal sequence has hardly any influence on potency or efficacy. The results with NDP-**MSH** and ACTH-(1-24) and the

other fragments lead the authors to postulate that it is not one of the five known subtypes of **melanocortin** receptors which mediates the hemodynamic effects of the **melanocortins**, but an addnl., still unidentified subtype. A clue for the elucidation of such a receptor might be found in the structural features of .gamma.-**MSH**-(6-12) that appear to be very important determinants for the effectiveness to alter peripheral and central hemodynamics.

L18 ANSWER 45 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:631423 HCAPLUS
DOCUMENT NUMBER: 125:317616
TITLE: Truncation studies of .alpha.-melanotropin peptides identify tripeptide analogs exhibiting prolonged agonist bioactivity
AUTHOR(S): Haskell-Luevano, Carrie; Sawyer, Tomi K.; Hendrata, Siska; North, Cheryl; Panahinia, Laila; Stum, Martha; Staples, Douglas J.; Castrucci, Anna M. De Lauro; Hadley, Mac E.; Hruby, Victor J.
CORPORATE SOURCE: Departments of Chemistry and Anatomy, Univ. of Arizona, Tucson, AZ, 85721, USA
SOURCE: Peptides (Tarrytown, New York) (1996), 17(6), 995-1002
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Systematic anal. of fragment derivs. of the superpotent .alpha.-**MSH** analog, Ac-Ser-Tyr-Ser-Nle4-Glu-His-D-Phe7-Arg-Trp-Gly-Lys-Pro-Val-NH2 (NDP-**MSH**), led to the discovery of tripeptide agonists possessing prolonged bioactivity in the frog skin assay. Of particular significance to this discovery was Ac-D-Phe-Arg-D-Trp-NH2, which was the most potent tripeptide in this series exhibiting sustained melanotropic activity. Different pharmacophore models appear to exist that are dependent on the substructure and stereochem. of the **MSH**(6-9) "active site.". The tripeptides Ac-D-Phe-Arg-Trp-NH2, Ac-D-Phe-Arg-D-Trp-NH2, and Ac-D-Phe-D-Arg-Trp-NH2 stereochem. combinations require only Phe7-Xaa8-Trp9, whereas Ac-D-Phe-D-Arg-D-Trp-NH2, Ac-Phe-Arg-D-Trp-NH2, and Ac-Phe-Arg-Trp-NH2 addnl. requires His6 for minimal biol. activity. Ac-D-Phe-Arg-D-Trp-NH2 represents a novel prototype lead for the development of **MSH**-based peptidomimetic agonists.

L18 ANSWER 46 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:373649 HCAPLUS
DOCUMENT NUMBER: 125:49681
TITLE: Involvement of calcium and cAMP in the mechanism of action of two **melanocortins**: .alpha. **MSH** and an ACTH-(4-9) analog
AUTHOR(S): Hol, Elly M.; Gispen, Willem-Hendrik; Bar, P. R.
CORPORATE SOURCE: Rudolf Magnus Institute, Utrecht University, Utrecht, 3584 CX, Neth.
SOURCE: Annals of the New York Academy of Sciences (1994), 739(Models of Neuropeptide Action), 324-327
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of .alpha.**MSH** and the ACTH 4-9 analog Org 2766 on second messengers were examd. in vitro in cells that are, in vivo, involved in peripheral nerve regeneration: spinal cord cells, dorsal root

ganglion cells, and Schwann cells. Results differed with the cell type used. Data indicated that the peptides stimulated different signal transduction pathways in spinal cord and dorsal root ganglion cells. It was concluded that cAMP formation may be a condition to trigger **melanocortin** receptors on these cell types. Interaction with other second messengers, esp. calcium, is needed to stimulate neurite outgrowth and the combination of second messenger systems needed probably depends on the receptor subtype in the cell.

L18 ANSWER 47 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:373626 HCAPLUS
DOCUMENT NUMBER: 125:49675
TITLE: Dorsal root ganglia as an in vitro model for **melanocortin**-induced neuritogenesis. Pharmacological and mechanistic aspects
AUTHOR(S): Hol, E. M.; Sodaar, P.; Bar, P. R.
CORPORATE SOURCE: Rudolf Magnus Institute, Utrecht University, Utrecht, 3584 CX, Neth.
SOURCE: Annals of the New York Academy of Sciences (1994), 739(Models of Neuropeptide Action), 74-86
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study, the authors focussed on the effects of .alpha.**MSH** and ACTH (4-9) analog Org 2766 in cultures of rat dorsal root ganglia (DGR). They investigated the neurotrophic activity after acute (1 h pretreatment) and chronic (48 h) treatment with these peptides and they studied the effect of the peptides on the stimulation of cAMP prodn. and c-fos expression in DGR cultures.

L18 ANSWER 48 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:7163 HCAPLUS
DOCUMENT NUMBER: 124:76685
TITLE: Cardiovascular effects of .gamma.-**MSH**/ACTH-like peptides: structure-activity relationship
AUTHOR(S): Van Bergen, Patricia; Janssen, Paul M. L.; Hoogerhout, Peter; De Wildt, Dick J.; Versteeg, Dirk H. G.
CORPORATE SOURCE: Department of Medical Pharmacology, Rudolf Magnus Institute for Neurosciences, Universiteitsweg 100, CG Utrecht, 3584, Neth.
SOURCE: European Journal of Pharmacology (1995), 294(2/3), 795-803
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB I.v. administration of .gamma.2-**MSH** to conscious rats causes a dose-dependent increase in blood pressure and heart rate, while the structurally related peptide adrenocorticotropic hormone-(4-10) (ACTH-(4-10)) is 5-10 times less potent in this respect. This prompted the authors' to investigate which amino acid sequence is determinant for the cardiovascular selectivity of peptides of the .gamma.-**MSH** family. Lys-.gamma.2-**MSH**, most likely the endogenously occurring .gamma.-**MSH** analog, was as potent as .gamma.2-**MSH** in inducing increases in blood pressure and heart rate. Removal of C-terminal amino acids resulted in .gamma.-**MSH** -fragments which were devoid of cardiovascular activities. Removal of amino acids from the N-terminal side of .gamma.2-**MSH** resulted in

fragments which were less potent, but had an intrinsic activity not different from that of .gamma.-**MSH**. Surprisingly, .gamma.-**MSH**-(6-12) was more potent than .gamma.2-**MSH**. The shortest fragment which displayed pressor and tachycardiac responses was the **MSH** 'core', His-Phe-Arg-Trp (= .gamma.-**MSH**-(5-8)), which is identical to ACTH-(6-9). This was corroborated by testing fragments of ACTH-(4-10). The authors conclude that the message essential for cardiovascular effects resides in the .gamma.-**MSH**-(5-8)/ACTH-(6-9) sequence. Proper C-terminal elongation is required for full expression of cardiovascular activity of .gamma.2-**MSH**, as the sequence of Asp9-Arg10-Phe11 appears to play an important role in establishing intrinsic activity. The amino acids N-terminal to the **MSH** 'core' sequence appear to be essential for the potency of the peptides.

L18 ANSWER 49 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:541833 HCAPLUS
DOCUMENT NUMBER: 122:307271
TITLE: **Melanocortin** analog Org 2766 binds to rat Schwann cells, upregulates NGF low-affinity receptor p75, and releases neurotrophic activity
AUTHOR(S): Dyer, J. K.; Philipsen, H. L. A.; Tonnaer, J. A. D. M.; Hermkens, P. H. H.; Haynes, Laurence W.
CORPORATE SOURCE: Sch. Biol. Sci., Univ. Bristol, Bristol, BS8 1UG, UK
SOURCE: Peptides (Tarrytown, New York) (1995), 16(3), 515-22
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Binding of the stable **melanocortin**(4-9) analog, Org 2766 [Met(O2)-Glu-His-Phe-D-Lys-Phe] to cultured rat sciatic nerve Schwann cells was demonstrated using a biotinylated deriv. in semiquant. histochem. and CELISA assays. Org 2766 bound to Schwann cells, but not to fibroblasts, and was displaced maximally by unlabeled Org 2766, .alpha.-**MSH** and ACTH(1-24). Displacement of Org 2766 from the binding sites was considerably reduced by N- and C-truncation of the peptide. Specific binding of Org 2766 was also demonstrated in the immortal rat Schwann cell line SCL4.1/F7 and was more pronounced in cells displaying a differentiated morphol. Org 2766 and .alpha.-**MSH** increased cAMP content of Schwann cells but neither stimulated DNA synthesis when applied alone. However, in the presence of a priming (subthreshold) concn. of the mitogen, cholera toxin, Org 2766 and .alpha.-**MSH** caused a delayed increase in DNA synthesis. Org 2766 did not modulate the expression of several differentiation-related Schwann cell markers. However, Org 2766 increased immunoreactivity for p75 low-affinity NGF receptor on Schwann cells and evoked the release of neurotrophic factor(s) that synergized with NGF in stimulating neurite outgrowth in rat DRG neurons. Apparently, Schwann cells are a primary target for the action of Org 2766 and provide evidence for an indirect mechanism by which **melanocortins** might stimulate neurite sprouting in regenerating peripheral nerve axons.

L18 ANSWER 50 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:296957 HCAPLUS
DOCUMENT NUMBER: 122:72399
TITLE: Differential effects of **melanocortin** peptides on neural **melanocortin** receptors
AUTHOR(S): Adan, Roger A. H.; Cone, Roger D.; Burbach, J. Peter H.; Gispen, Willem Hendrik

Search completed by David Schreiber 308-4292

CORPORATE SOURCE: Rudolf Magnus Institute for Neuroscience, Utrecht Univ., Utrecht, 3508 TA, Neth.
SOURCE: Molecular Pharmacology (1994), 46(6), 1182-90
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Melanocortins** (MCs) have various physiol. actions on the brain. The recent cloning of neural MC receptors opened new avenues to study the effects of these neuropeptides on the nervous system. Here the authors investigated the structure-activity relationships (SARs) of peptides derived from adrenocorticotropic hormone (ACTH) with cloned MC3 and MC4 receptors in vitro and correlated the with central effects of MCs in vivo. Anal. of the effects of various MC peptides on cAMP accumulation in and binding to cells that expressed either the rat MC3 receptor or the human MC4 receptor demonstrated that ACTH-4-9-NH2 was the core sequence of ACTH able to activate these receptors. Furthermore, .gamma.-**MSH** displayed selectivity for the MC3 receptor, whereas [D-Phe7]ACTH-4-10 more efficiently activated the MC4 receptor than the MC3 receptor. The activities of MC fragments that lacked the three carboxyl-terminal amino acids (residues 11-13) of ACTH1-13 were much lower than that of .alpha.-**MSH**, for both receptors. Furthermore, the three amino-terminal amino acids (residues 1-3) of .alpha.-**MSH** were more important for full activation of the MC4 receptor, compared with the MC3 receptor. The SAR for the MC4 receptor resembled that for the induction of excessive grooming behavior by MC peptides. Therefore, the authors suggest that this behavioral response is mediated by MC4 receptors. The SAR for the MC3 receptor did not overlap with that for in vivo effects of MCs. ORG2766, an ACTH-4-9 analog that is very potent in an active avoidance task, did not activate, antagonize, or bind to the MC3 and MC4 receptors. This suggests the presence of still other MC receptors, in addn. to the MC3 and MC4 receptors, in the brain. These data identify peptides with selectivity for either the MC3 receptor or the MC4 receptor, which may be used for development of novel MC receptor-specific ligands. Furthermore, this is the first report that discusses behavioral effects of MCs in light of data on cloned MC receptors.

L18 ANSWER 51 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:401838 HCAPLUS
DOCUMENT NUMBER: 121:1838
TITLE: The effect of nerve growth factor, ciliary neurotrophic factor, and ACTH analogs on cisplatin neurotoxicity in vitro
AUTHOR(S): Windebank, Anthony J.; Smith, A. Gordon; Russell, James W.
CORPORATE SOURCE: Cell. Neurobiol. Lab., Dep. Neurol., Rochester, MN, USA
SOURCE: Neurology (1994), 44(3, PT. 1), 488-94
CODEN: NEURAI; ISSN: 0028-3878
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cisplatin, used to treat ovarian, bladder, and testicular cancers, causes a sensory dose-limiting neuropathy. Preliminary observations in humans and animals suggest that nerve damage may be prevented by ACTH analogs, particularly those belonging to the **melanocortin** class, and by nerve growth factor (NGF). The authors established a rat embryo dorsal root ganglion model to study cisplatin neurotoxicity. The drug reproducibly inhibited axonal growth at concns. similar to that known to produce toxicity in neurons. The inhibition was prevented in a

dose-dependent fashion by simultaneous exposure to .alpha.-**MSH** or ACTH4-9 but not by excess NGF or ciliary neurotrophic factor (CNTF). The ACTH peptides were not effective in preventing suramin-induced neurotoxicity in the same model. Drug interaction and dose-response studies showed that ACTH4-9 and .alpha.-**MSH** do not act by potentiation of NGF action. ACTH analogs appear to protect against cisplatin-induced neurotoxicity directly at the cellular level.

L18 ANSWER 52 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:552246 HCAPLUS
DOCUMENT NUMBER: 119:152246
TITLE: Structure-activity relationships of [Nle4, D-Phe7].alpha.-**MSH**. Discovery of a tripeptidyl agonist exhibiting sustained bioactivity
AUTHOR(S): Sawyer, Tomi K.; Castrucci, Ana M.; Staples, Douglas J.; Affholter, Joseph A.; De Vaux, Anne E.; Hruby, Victor J.; Hadley, Mac E.
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Annals of the New York Academy of Sciences (1993), 680(Melanotropic Peptides), 597-9
CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors examd. the entire [Nle4,D-Phe7].alpha.-**MSH** (NDP-**MSH**) mol. and prepd. a series of N-terminal fragments, C-terminal fragments, and addnl. internal fragments all of which incorporated a D-Phe-7 moiety. These studies have identified D-Phe-Arg-Trp as the minimal sequence of NDP-**MSH** effective as an agonist and exhibiting sustained-acting properties using skin bioassays.

L18 ANSWER 53 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:140048 HCAPLUS
DOCUMENT NUMBER: 118:140048
TITLE: ACTH: A structure-activity study on pilocarpine-induced epilepsy
AUTHOR(S): Croiset, Gerda; De Wied, David
CORPORATE SOURCE: Med. Fac., Univ. Utrecht, Utrecht, Neth.
SOURCE: European Journal of Pharmacology (1993), 229(2-3), 211-16
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intracerebroventricularly applied pilocarpine (2.4 mg/2 .mu.L) immediately produced symptoms of epilepsy, ranging from akinesia to motor seizures, in rats. ACTH-(1-39), ACTH-(1-24), ACTH-(1-18), ACTH-(1-16), and ACTH-(18-39) were not active, but s.c. pretreatment with smaller ACTH-like fragments, such as ACTH-(4-9), ACTH-(4-10), ACTH-(4-10)(7D-Phe), ACTH-(7-16), and Org 2766, reduced the severity of the epilepsy. Moreover, fewer rats developed motor seizures. Thus, ACTH fragments devoid of peripheral endocrine activity reduced pilocarpine-induced epileptiform activity in rats. A narrow bell-shaped dose-response relationship was found. Except for ACTH-(7-16), which was active in a dose of 1 or 10 .mu.g/rat s.c., the other fragments were only active at 10 .mu.g/rat. The antiepileptic properties appeared to reside in the sequence 1-16, and more specifically in the sequences 4-7 and 7-16, of the ACTH mol.

L18 ANSWER 54 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:585204 HCAPLUS

DOCUMENT NUMBER: 117:185204
TITLE: ACTH/**MSH** like peptides in the treatment of cisplatin neuropathy
AUTHOR(S): Gispen, W. H.; Hamers, F. P. T.; Vecht, C. J.; Jennekens, F. G. I.; Neyt, J. P.
CORPORATE SOURCE: Rudolf Magnus Inst., State Univ. Utrecht, Utrecht, 3521 GD, Neth.
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1992), 43(1-3), 179-83
CODEN: JSBBEZ; ISSN: 0960-0760
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The neurol. toxicity seen in patients treated with cisplatin in most cases concerns ototoxicity and peripheral neuropathy. Thus far, the pathogenesis of cisplatin neuropathy remains obscure. The fact that cisplatin affects mainly the sensory peripheral nerve fibers points towards an involvement of the dorsal root ganglia. In a rat model of cisplatin neuropathy, following a cumulative dose of approx. 12 mg/kg of cisplatin, the sensory nerve conduction velocity began to slow as compared to age-matched controls. Peptides derived from ACTH and **MSH** are known to exert neurotrophic effects. In vivo they facilitate postlesion repair mechanisms in the peripheral nervous system by enhancing the early sprouting response of the damaged nerve. Surprisingly, chronic treatment with a synthetic ACTH4-9 analog not only prevented cisplatin neurotoxicity following a low or high dose regimen, but also counteracted already existing cisplatin-induced neurotoxicity. Stimulated by these findings a randomized, double blind, placebo-controlled study was performed to assess the efficacy of the peptide in the prevention of cisplatin neuropathy in women suffering from ovarian cancer. The threshold of vibration perception (VPT) was used as the principal measure of neurotoxicity. Following 6 cycles of chemotherapy the VPT had increased > 8-fold in women receiving placebo as co-medication. Whereas the VPT in women receiving 1 mg/m2 body surface ACTH4-9 analog before and after each cisplatin cycle only increased <2-fold. No side effects of the peptide treatment were obsd. and the clin. response to the chemotherapy was similar in all treatment groups. Collectively these preclin. and clin. data suggest that treatment based on non-endocrine fragments of ACTH/**MSH** may be a therapeutic option in the treatment of cisplatin neuropathy.

L18 ANSWER 55 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:551287 HCAPLUS
DOCUMENT NUMBER: 115:151287
TITLE: Serotonin binding sites. II. Muramyl dipeptide binds to serotonin binding sites on myelin basic protein, LH-RH, and **MSH**-ACTH 4-10
AUTHOR(S): Root-Bernstein, Robert Scott; Westall, Fred C.
CORPORATE SOURCE: Dep. Physiol., Michigan State Univ., East Lansing, MI, 48824, USA
SOURCE: Brain Research Bulletin (1990), 25(6), 827-41
CODEN: BRBUDU; ISSN: 0361-9230
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The existence of structurally similar serotonin binding sites on myelin basic protein, HRH, and **MSH**-ACTH 4-10 has been reported. This report shows that the adjuvant peptide, muramyl dipeptide also binds to these sites. This observation may help to explain previous observations of serotonin-like activity by muramyl peptides, including the promotion of slow-wave sleep and fever induction. The observation may also provide an important link between the immune system and the nervous system that may

explain the role of muramyl dipeptide adjuvants in causing autoimmune diseases to serotinin-regulated proteins and their receptors, as well as the alterations in serotonin levels that are often obsd. in autoimmune diseases. The observation provides concrete evidence for a dual-antigen hypothesis for the induction of autoimmune diseases by an adjuvant-peptide complex. Application of such a mechanism for induction of autoimmunity may be of importance in understanding a no. of postinfectious and postvaccinal neuropathies, and suggests a possible etiol. for autism, in which many patients have high blood serotonin levels, autoimmune reactions to myelin basic protein, and antibodies to serotonin binding sites. Finally, the observation suggests that glycopeptides may act as neurotransmitters.

L18 ANSWER 56 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:506305 HCAPLUS
DOCUMENT NUMBER: 115:106305
TITLE: ACTH/**MSH**-like peptides inhibit the binding of dopaminergic ligands to the dopamine D2 receptor in vitro
AUTHOR(S): Florijn, Wouter J.; De Boer, Thijs; Tonnaer, Jeroen A. D. M.; Van Nispen, Jan W.; Versteeg, Dirk H. G.
CORPORATE SOURCE: Med. Fac., Univ. Utrecht, Utrecht, 3521 GD, Neth.
SOURCE: European Journal of Pharmacology, Molecular Pharmacology Section (1991), 207(1), 43-50
CODEN: EJPPET; ISSN: 0922-4106
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ACTH-(1-24) decreased the binding of the dopamine D2 receptor agonist, [3H]N-propylnorapomorphine ([3H]NPA), to rat striatal membranes in a concn.-dependent manner, with a Ki of 5 .times. 10-7M. Satn. curves for [3H]NPA binding in the presence of increasing concns. of ACTH-(1-24) were performed. Scatchard anal. in the presence of ACTH-(1-24) revealed an increased dissocn. const. (Kd), while the binding capacity (Bmax) was not affected by the peptide, suggesting an apparent competitive interaction between ACTH-(1-24) and [3H]NPA. ACTH-(1-24) also reduced the binding of the dopamine D2 receptor antagonist [3H]spiperone to striatal membranes, with a Ki of 10-6M. Much higher concns. of ACTH-(1-24), up to 10-4M, were needed for the displacement of appropriate radiolabeled ligands from dopamine D1 receptors, serotonin 5-HT1A, serotonin 5-HT1B, muscarinic M1 acetylcholine, and histamine H1 receptors. ACTH-(1-24) also inhibited the binding of [3H]spiperone to dopamine D2 receptors in membranes of the pituitary gland, the septum and the substantia nigra. ACTH-(1-39) and most ACTH fragments and analogs were less potent than ACTH-(1-24) in displacing [3H]NPA from the dopamine D2 receptor in striatal membranes. In general there was a relationship between displacing potency and chain length. ACTH-(7-16)-NH2 and benzyloxycarbonyl-ACTH-(8-16)-NH2, however, were more potent than ACTH-(1-24) in reducing the binding of [3H]NPA to dopamine D2 receptors. ACTH-(7-16)-NH2 appeared to contain the minimal required amino acid sequence for inhibition of [3H]NPA binding, because a further shortening of the peptide resulted in a marked decrease of inhibitory potency. The present data show that ACTH/**MSH**-like peptides preferentially interact with dopamine D2 receptors.

L18 ANSWER 57 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:423130 HCAPLUS
DOCUMENT NUMBER: 115:23130
TITLE: Putative neurotropic factors and functional recovery from peripheral nerve damage in the rat
AUTHOR(S): Van der Zee, Catharina E. E. M.; Brakkee, Jan H.;

Gispen, Willem Hendrik
CORPORATE SOURCE: Med. Fac., Univ. Utrecht, Utrecht, 3521 GD, Neth.
SOURCE: British Journal of Pharmacology (1991), 103(1), 1041-6
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In rats, recovery of sensory motor function following a crush lesion of the sciatic or tibial nerve was monitored by measuring foot reflex withdrawal from a local noxious stimulation of the foot sole. Putative neurotropic compds. were tested on this functional recovery model: **melanocortins** (peptides derived from ACTH and .alpha.-**MSH**), gangliosides and nimodipine were effective, whereas isaxonine and TRH were not. Structure-activity studies with **melanocortins** revealed a similar effectiveness of .alpha.-**MSH**, [N-Leu4, D-Phe7]-.alpha.-**MSH**, desacetyl-.alpha.-**MSH**, and the ACTH4-9 analog ORG 2766, questioning the validity of the previously suggested notion that the melanotropic properties of these peptides are responsible for their neurotropic effect. As recovery of function after peripheral nerve damage follows a similar time course in hypophysectomized (5 days post operation) and sham-operated rats, effective **melanocortin** therapy does not mimic an endogenous peptide signal in the repair process from pituitary origin. S.c. treatment with ORG 2766 (7.5 .mu.g/kg/48 h) facilitates recovery of function following peripheral nerve damage in young (6-7-wk-old), mature (5-mo-old), and old (20-mo-day) rats. In view of the diversity in structure of the effective neurotropic factors and the complexity of nerve repair, the present data support the notion that peripheral nerve repair may be facilitated by different humoral factors likely to be active on different aspects of the recovery process.

L18 ANSWER 58 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:417963 HCAPLUS
DOCUMENT NUMBER: 113:17963
TITLE: .alpha.-**Melanocyte** stimulating hormone message and inhibitory sequences: comparative structure-activity studies on **melanocytes**
AUTHOR(S): Sawyer, Tomi K.; Staples, Douglas J.; Castrucci, Ana M. L.; Hadley, Mac E.; Al-Obeidi, Fahad A.; Cody, Wayne L.; Hruby, Victor J.
CORPORATE SOURCE: Pept. Ther. Core Facil., Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Peptides (New York, NY, United States) (1990), 11(2), 351-7
CODEN: PPTDD5; ISSN: 0196-9781
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The structure-activity relationships of .alpha.-**MSH** fragment derivs. of the generic formulae Ac-.alpha.-**MSH**(x-13)-NH2 and Ac-.alpha.-**MSH**(6-x)-NH2 were investigated. The minimal C-terminal sequences required for melanotropic activity were 8-13 and 7-13, resp., in the frog and lizard skin bioassays. The Arg8-Trp9 sequence appeared to be a fundamental component of the minimal message sequences found, such as .alpha.-**MSH**(6-9), .alpha.-**MSH** (8-13), and .alpha.-**MSH**(7-13). Ac-.alpha.-**MSH** (7-13)-NH2 was a weak and selective .alpha.-**MSH** antagonist on the lizard skin bioassay. Anal. of .alpha.-**MSH**(7-10) analogs of the generic formula Ac-X-Arg-Trp-Y-NH2 indicated that Ac[D-Trp7,D-Phe10].alpha.-**MSH**(7-13)-NH2 was a moderately potent, specific, and competitive inhibitor of .alpha.-**MSH** in both the frog and

the lizard skin bioassays.

L18 ANSWER 59 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:421139 HCAPLUS
DOCUMENT NUMBER: 111:21139
TITLE: Melanotropin structure-activity studies on **melanocytes** of the teleost fish, Synbranchus marmoratus
AUTHOR(S): Castrucci, Ana Maria de L.; Hadley, Mac E.; Wilkes, Brian C.; Hruby, Victor J.; Sawyer, Tomi K.
CORPORATE SOURCE: Inst. Biocienc., Univ. Sao Paulo, Sao Paulo, 05499, Brazil
SOURCE: General and Comparative Endocrinology (1989), 74(2), 209-14
CODEN: GCENA5; ISSN: 0016-6480
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The minimal sequence of .alpha.-**MSH** required for full agonism on fish (S. marmoratus) **melanocytes** was Ac-.alpha.-MSH5-10-NH2 since Ac-.alpha.-MSH6-10-NH2 and Ac-.alpha.-MSH6-9-NH2 were inactive. The N-terminal tripeptide sequence, Ser-Tyr-Ser, lacked any contribution to potency since the 4-13 (Ac-[Nle4]-.alpha.-MSH4-13-NH2) sequence was equipotent to .alpha.-**MSH**. The important potentiating amino acids were methionine at position 4 of the N-terminus and valine at position 13 of the C-terminus of the hormone, since Ac-.alpha.-MSH4-10-NH2 was about 100 times more potent than the Ac-.alpha.-MSH5-10-NH2 sequence, and Ac-[Nle4]-.alpha.-MSH4-13-NH2 was 10 times more active than Ac-[Nle4]-.alpha.-MSH4-12-NH2. The minimal sequence for equipotency to .alpha.-**MSH** was Ac-[Nle4]-.alpha.-MSH4-13-NH2. [Nle4,D-Phe7]-.alpha.-**MSH** was about 10 times more active than .alpha.-**MSH**. Unexpectedly, several conformationally restricted cyclic melanotropins were either partial agonists (cyclic [Cys4,Cys10]-.alpha.-**MSH**) or totally inactive (cyclic Ac[Cys4,Cys10]-.alpha.-MSH4-10-NH2) on fish **melanocytes**. These results point out some rather remarkable differences between S. marmoratus and tetrapod melanophores relative to structural requirements for **MSH** receptor recognition and signal transduction.

L18 ANSWER 60 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:88954 HCAPLUS
DOCUMENT NUMBER: 110:88954
TITLE: .alpha.-Melanotropin: the minimal active sequence in the lizard skin bioassay
AUTHOR(S): Castrucci, A. M. L.; Hadley, M. E.; Sawyer, T. K.; Wilkes, B. C.; Al-Obeidi, F.; Staples, D. J.; De Vaux, A. E.; Dym, O.; Hintz, M. F.; et al.
CORPORATE SOURCE: Inst. Biocienc., Univ. Sao Paulo, Sao Paulo, 05499, Brazil
SOURCE: General and Comparative Endocrinology (1989), 73(1), 157-63
CODEN: GCENA5; ISSN: 0016-6480
DOCUMENT TYPE: Journal
LANGUAGE: English
AB .alpha.-Melanotropin (.alpha.-**MSH**) is a tridecapeptide, Ac-Ser-Tyr-Ser-Met-Glu-His-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH2. The minimal sequence of .alpha.-**MSH** required for agonism in the lizard (Anolis carolinensis) skin bioassay was detd. to be Ac-His-Phe-Arg-Trp-NH2 (Ac-.alpha.-MSH6-9-NH2). Smaller fragments of this sequence (Ac-.alpha.-MSH6-8-NH2, Ac-.alpha.-MSH6-7-NH2, Ac-.alpha.-MSH7-9-NH2, and

Ac-.alpha.-MSH7-8-NH2) were devoid of melanotropic activity. The tetrapeptide Ac-.alpha.-MSH7-10-NH2 was also inactive, thus again demonstrating the importance of His at position 6 for minimal activity. The important potentiating amino acids were Met-4, Lys-11, and Pro-12, since Ac-.alpha.-MSH4-10-NH2 was about 100 times more potent than Ac-.alpha.-MSH5-10-NH2, and Ac-[Nle4]-.alpha.-MSH4-11-NH2 was about 40 times more potent than Ac-.alpha.-MSH4-10-NH2 or Ac-[Nle4]-.alpha.-MSH4-10-NH2. Ac-.alpha.-MSH4-12-NH2 and Ac-[Nle4]-.alpha.-MSH4-12-NH2 were equipotent and about 6 times more potent than .alpha.-**MSH**. Since [Nle4]-.alpha.-**MSH** and Ac-[Nle4]-.alpha.-MSH4-13-NH2 were both equipotent but about sixfold less active than Ac-[Nle4]-.alpha.-MSH4-12-NH2, it is clear that valine at position 13 does not contribute to the potency of .alpha.-**MSH**, except possibly in a neg. way. The minimal message sequence for equipotency to .alpha.-**MsH** appears to be Ac-Met-Glu-His-Phe-Arg-Trp-Gly-Lys-NH2, since the analog, Ac-[Nle4]-.alpha.-MSH4-11-NH2, was as active as the native hormone. Ser-1, Tyr-2, Ser-3, Glu-5, and Val-13 are not important for melanotropic potency since Ac-.alpha.-MSH4-12-NH2 was more potent than .alpha.-**MSH**, and Ac-.alpha.-MSH5-10-NH2 and Ac-.alpha.-MSH6-10-NH2 were equipotent, being about 4000 times less active than .alpha.-**MSH**.

L18 ANSWER 61 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:19047 HCAPLUS
DOCUMENT NUMBER: 110:19047
TITLE: Use of melanotropin or its peptide fragments for the treatment of asthmatic and allergic diseases
INVENTOR(S): Aderhold, Dieter
PATENT ASSIGNEE(S): Fed. Rep. Ger.
SOURCE: Ger. Offen., 3 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3623019	A1	19880121	DE 1986-3623019	19860709

PRIORITY APPLN. INFO.: DE 1986-3623019 19860709
AB .alpha.-**MSH**, .beta.-**MSH**, .gamma.-**MSH**, and/or their peptide fragments are useful for the treatment of allergic or asthmatic diseases. A dermally applied compn. contained 2 mg melanotropin tetrapeptide (His-Phe-Arg-Trp) colloidally adsorbed to 12 mg Al(OH)3, a swell as 13 mL water and 7 mL EtOH. This compn. was applied to the nostrils and the areas over the sinuses and >90% of the patients showed a decrease in the symptoms related to hay fever and dust allergies.

L18 ANSWER 62 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:107130 HCAPLUS
DOCUMENT NUMBER: 108:107130
TITLE: Method and composition for stimulating **melanocytes** by topical application of alpha-**MSH** and analogs
INVENTOR(S): Hruby, Victor J.; Hadley, Mac E.; Dorr, Robert; Levine, Norman
PATENT ASSIGNEE(S): University Patents, Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

Search completed by David Schreiber 308-4292

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8704623	A1	19870813	WO 1987-US226	19870123
W: AU, DK, HU, JP, KR, RO, SU				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8770828	A1	19870825	AU 1987-70828	19870123
AU 597630	B2	19900607		
EP 259440	A1	19880316	EP 1987-901815	19870123
EP 259440	B1	19930113		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 63502894	T2	19881027	JP 1987-501451	19870123
JP 06011710	B4	19940216		
AT 84420	E	19930115	AT 1987-901815	19870123
CA 1282324	A1	19910402	CA 1987-528829	19870203
DK 8705181	A	19871202	DK 1987-5181	19871002
US 4918055	A	19900417	US 1988-154823	19880211
US 4866038	A	19890912	US 1988-224187	19880722
US 5049547	A	19910917	US 1989-340305	19890419

PRIORITY APPLN. INFO.:
US 1986-825162 19860203
EP 1987-901815 19870123
WO 1987-US226 19870123
US 1988-154823 19880211

AB A method for stimulating melanin prodn. in a mammal comprises topical administration of .alpha.-**MSH** and/or analogs. [Nle4,D-Phe7]-.alpha.-**MSH** was dissolved in PEG (26% PEG 400, 74% PEG 3350 by wt.) at 10-6M and the ointment was applied topically to the skin of plucked mice. Microscopic examn. revealed eumelanin within hair bulbs by 24 h following application of the analog. Follicular melanogenesis was not restricted to the hair bulbs of the treated site but was obsd. microscopically in hair bulbs taken from untreated areas of the animal where hair growth was in progress.

L18 ANSWER 63 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:576467 HCAPLUS
DOCUMENT NUMBER: 107:176467
TITLE: .alpha.-Melanotropin: the minimal active sequence in the frog skin bioassay
AUTHOR(S): Hruby, Victor J.; Wilkes, Brian C.; Hadley, Mac E.; Al-Obeidi, Fahad; Sawyer, Tomi K.; Staples, Douglas J.; DeVaux, Ann E.; Dym, Orin; Castrucci, Ana Maria de L.; et al.
CORPORATE SOURCE: Dep. Chem., Univ. Arizona, Tucson, AZ, 85721, USA
SOURCE: Journal of Medicinal Chemistry (1987), 30(11), 2126-30
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:176467
GI

Ac-Ser-Tyr-Ser-Met-Glu-His-Phe-
Arg-Trp-Gly-Lys-Pro-Val-NH_2 I

Search completed by David Schreiber 308-4292

Kam 10/040,547

AB A series of fragment analogs of .alpha.-**MSH** (I) were prepd. in order to det. the contribution of each individual amino acid to the biol. activity of the native hormone. The minimal potency of Ac-.alpha.-MSH6-9-NH2 could be enhanced about a factor of 16 by the addn. of glycine to the C-terminus, yielding Ac-.alpha.-MSH6-10-NH2. Addn. of glutamic acid to the N-terminus provided Ac-.alpha.-MSH5-10-NH2, which was only slightly more potent than Ac-.alpha.-MSH6-10-NH2, indicating that position 5 contributes little to the biol. potency of .alpha.-**MSH** in this assay. Addn. of methionine to the N-terminus of Ac-.alpha.-MSH5-10-NH2 resulted in Ac-.alpha.-MSH4-10-NH2, which was only about 4-fold more potent than Ac-.alpha.-MSH5-10-NH2. Addn. of lysine and proline to the C-terminal of the Ac-.alpha.-MSH4-10-NH2 sequence yielded Ac-.alpha.-MSH4-12-NH2 with a 360-fold increase in potency relative to Ac-.alpha.-MSH4-10-NH2. This peptide was only about 6-fold less potent than .alpha.-**MSH**. Nle-4-substituted analogs were also prepd. Ac-[Nle4]-.alpha.-MSH4-10-NH2 and Ac-[Nle4]-.alpha.-MSH4-11-NH2 were .apprx.4 times more potent than Ac-.alpha.-MSH4-10-NH2, demonstrating that lysine-11 contributes somewhat to the biol. activity of .alpha.-**MSH** on the frog skin **melanocyte** receptor. However, addn. of proline-12 to this fragment, yielding Ac-[Nle4]-.alpha.-MSH4-12-NH2, resulted in about a 90-fold increase in relative potency of the melanotropin. Addn. of the final C-terminal valine-13 provided Ac-[Nle4]-.alpha.-MSH4-13-NH2, which showed only a small further increase in potency. This analog was, however, only about 2 to 3-fold less active than .alpha.-**MSH**. Addn. of the N-terminal tripeptide Ac-Ser-Tyr-Ser to yield [Nle4]-.alpha.-**MSH** resulted in an analog that was 3 times more potent than .alpha.-**MSH**. The central tetrapeptide sequence, Ac-His-Phe-Arg-Trp-NH2, represents the min. chain length for observable biol. activity. The active sequence of .alpha.-**MSH** is contiguous in that no two structurally noncontiguous fragment sequences were found to have biol. activity. Met-4, Gly-10, and Pro-12 are important potentiating amino acids and contribute significantly to the biopotency of .alpha.-**MSH**, and Ser-1 and -3, Tyr-2, Glu-5, Lys-11, and Val-13 apparently contribute only minimally to the biol. potency of .alpha.-**MSH** at the frog **melanocyte** skin receptor.

L18 ANSWER 64 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:491517 HCAPLUS
DOCUMENT NUMBER: 105:91517
TITLE: Potent and prolonged melanotropic activities of the .alpha.-**MSH** fragment analog, Ac-[Nle4, D-Phe7]-.alpha.-MSH4-9-NH2
AUTHOR(S): Klemes, David G.; Kreutzfeld, Kristie L.; Hadley, Mac E.; Cody, Wayne L.; Hruby, Victor J.
CORPORATE SOURCE: Dep. Anat., Univ. Arizona, Tucson, AZ, 85724, USA
SOURCE: Biochemical and Biophysical Research Communications (1986), 137(2), 722-8
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ac-[Nle4,D-Phe7]-.alpha.-MSH4-9-NH2 [**103827-19-6**] and Ac-[Nle4]-.alpha.-MSH4-9-NH2 [**103882-77-5**] fragment analogs of .alpha.-**MSH** were synthesized. The potency and prolonged activity of the analogs were compared with effects of .alpha.-**MSH** in several melanotropin bioassays. The D-phenylalanine-contg. hexapeptide was 10-fold more active than .alpha.-**MSH** in stimulating melanoma tyrosinase [9002-10-2] activity. This analog was also 10-fold more

Search completed by David Schreiber 308-4292

potent than .alpha.-**MSH** in the lizard skin bioassay and about 10-fold less active in the frog skin bioassay. The melanotropic activity of Ac-[Nle4,-D-Phe7]-.alpha.-MSH4-9-NH2 was considerably prolonged compared with that of .alpha.-**MSH** in each of the bioassays. These results demonstrate that the structural requirements for superpotency and prolonged activity of [Nle4,-D-Phe7]-substituted analogs reside within this hexapeptide sequence.

L18 ANSWER 65 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:29121 HCAPLUS
DOCUMENT NUMBER: 104:29121
TITLE: ACTH 4-9 effects on the human visual event-related potential
AUTHOR(S): Sandman, Curt A.; Berka, Chris; Walker, Barbara B.; Veith, Jane
CORPORATE SOURCE: Dep. Psychiatry, Univ. California, Irvine, CA, USA
SOURCE: Peptides (New York, NY, United States) (1985), 6(5), 803-7
CODEN: PPTDD5; ISSN: 0196-9781
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ACTH-4-9 [**56236-83-0**] (5-20 mg) was administered to human subjects and effects on 4 visual event-related potentials (ERPs) were studied. Dose, time after administration, hemisphere of the brain from which ERPs were recorded, and sex influenced ERPs. The ACTH analog decreased the amplitude of early components but increased integrated activity of the ERP. This effect peaked at 60 min then recovered. The effects of the peptide were more pronounced with doses of 5 and 10 mg, in the right hemisphere of men, and in the left hemisphere of women. Thus, ACTH-4-9 influences components of the ERP related to the perceptual/attentional state in a **sexually** dimorphic manner.

L18 ANSWER 66 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:554871 HCAPLUS
DOCUMENT NUMBER: 103:154871
TITLE: Melanotropin and peptides for treatment of multiple sclerosis, nervous diseases, and skin diseases
INVENTOR(S): Aderhold, Dieter
PATENT ASSIGNEE(S): Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 146113	A2	19850626	EP 1984-115260	19841212
EP 146113	A3	19870819		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
DE 3345358	A1	19850627	DE 1983-3345358	19831215
DE 3345397	A1	19850627	DE 1983-3345397	19831215
DE 3424009	A1	19860102	DE 1984-3424009	19840629

PRIORITY APPLN. INFO.: DE 1983-3345358 19831215
DE 1983-3345397 19831215
DE 1984-3424009 19840629

AB Prepns. contg. .alpha.-**MSH** [37213-49-3], .beta.-**MSH** [9034-42-8], and(or) .gamma.-**MSH** [72711-43-4] were effective

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therapeutic agents for treating multiple sclerosis, diseases of the nervous system, rheumatic diseases, and skin disorders. Other prepns. also contained, in addn. to the melanotropins, peptide fragments of these hormones.

L18 ANSWER 67 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:554287 HCAPLUS
DOCUMENT NUMBER: 103:154287
TITLE: Corticotropin-peptide regulation of intracellular cyclic AMP production in cortical neurons in primary culture
AUTHOR(S): Weiss, Samuel; Sebben, Michele; Bockaert, Joel
CORPORATE SOURCE: CNRS, INSERM, Montpellier, 34003, Fr.
SOURCE: Journal of Neurochemistry (1985), 45(3), 869-74
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In neurons of the mouse cerebral cortex in primary culture, ACTH peptides stimulated cAMP [60-92-4] synthesis .ltoreq.3-fold in a dose-dependent manner; stimulation was complete within 5-10 min of exposure to agonists. Neurohormone efficacy was augmented by 0.1 .mu.M forskolin (which was virtually ineffective alone); potency was unaffected. The order of potency (50% effective concn.) for increasing intracellular cAMP levels was as follows: 1-24-ACTH [16960-16-0], 1-17-ACTH [7266-47-9] (10 nM) > .alpha.-**MSH** [37213-49-3], .beta.-**MSH** [9034-42-8] (100 nM) > 1-10-ACTH [2791-05-1] (1 .mu.M) > 4-10-ACTH [4037-01-8] (5 .mu.M). 4-9-ACTH [**56236-83-0**] as well as 11-24-ACTH [4237-93-8] were inactive at concns. .ltoreq.10 .mu.M. Other neuropeptides derived from proopiocortin, such as .beta.-endorphin and methionine and leucine-enkephalin were without effect on basal or hormonally stimulated cAMP synthesis. To det. whether distinct receptors for ACTH are present on cortical neurons, satg. concns. of the peptide were coincubated with either VIP or the .beta.-adrenergic agonist, isoproterenol (INE). The response to combinations of ACTH and INE were clearly additive. However, neither ACTH nor INE could further augment cAMP formation at satg. concns. of VIP. Comparison of structure-activity relations suggest that ACTH receptors mediating the elevation of cAMP formation in cortical neurons may be similar to those assocd. with the peptide actions on arousal rather than conditioned behavior.

L18 ANSWER 68 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:564048 HCAPLUS
DOCUMENT NUMBER: 101:164048
TITLE: Regenerative action of ACTH on damaged nerve fibers
AUTHOR(S): Gispen, W. H.; Bijlsma, W. H.; Jennekens, F. G. I.; Schotman, P.
CORPORATE SOURCE: Neth.
SOURCE: Organorama (1984), 21(2), 3-6, 9
CODEN: ORGNA4; ISSN: 0369-7762
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The s.c. injection of ACTH [9002-60-2], ACTH(1-24) [16960-16-0], ACTH(4-10) [4037-01-8], ACTH(4-9) [**56236-83-0**], and ACTH(6-10) [2279-03-0] increased functional recovery after sciatic nerve crush injury in rats, as assessed by return of a pain-induced abduction reflex in the leg. .alpha.-**MSH** [37213-49-3], which is structurally similar to ACTH(1-13), also increased the speed of functional recovery. On histol. examn. of the sciatic nerve, more regenerating myelinated axons were present when ACTH(4-10) was administered after the crush injury than

in controls. All other regenerating axons were also stimulated by ACTH(4-10). However, the diams. and the growth rates of the regenerating axons were not altered by ACTH(4-10). Injection of small ACTH fragments such as ACTH(1-16) [5576-42-1] and ACTH(4-10) increased the amino acid uptake in lumbar spinal cord of control rats, but no increase in the rats of total protein formation was seen in the lumbar spinal cord in response to ACTH(4-10) after sciatic nerve crush injury. However, with ACTH(4-10), there was a shift toward the formation of structural proteins, such as actin and tubulin, in the lumbar spinal cord after sciatic nerve crush injury. The possible therapeutic use of ACTH-like peptides in regeneration of peripheral nerves is discussed.

L18 ANSWER 69 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:563847 HCAPLUS
DOCUMENT NUMBER: 101:163847
TITLE: Effect of small peptides, ACTH fragments, on phosphorus-32 incorporation in brain proteins in vitro
AUTHOR(S): Cehovic, Georges; Cassonnet, Patricia
CORPORATE SOURCE: Fac. Pharm., Univ. Paris-Sud, Chatenay-Malabry, 92290, Fr.
SOURCE: Comptes Rendus de l'Academie des Sciences, Serie III: Sciences de la Vie (1984), 298(7), 191-4
CODEN: CRASEV; ISSN: 0764-4469
DOCUMENT TYPE: Journal
LANGUAGE: French
AB ACTH (4-10) [4037-01-8] increased 32P incorporation into rat brain protein in vitro, whereas ACTH (6-9) [**4289-02-5**] inhibited the phosphorylation and ACTH [9002-60-2], .alpha.-**MSH** [37213-49-3], ACTH (1-4) [19405-50-6], and ACTH (5-10) [4086-29-7] were without effect. The possibility that ACTH fragments play a role in the regulation of some brain functions through different protein kinases is discussed.

L18 ANSWER 70 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:484125 HCAPLUS
DOCUMENT NUMBER: 101:84125
TITLE: Serotonin binding sites. I. Structures of sites on myelin basic protein, LH-RH, **MSH**, ACTH, interferon, serum albumin, ovalbumin and red pigment concentrating hormone
AUTHOR(S): Root-Bernstein, Robert Scott; Westall, Fred C.
CORPORATE SOURCE: Salk Inst. Biol. Stud., San Diego, CA, 92138-9216, USA
SOURCE: Brain Research Bulletin (1984), 12(4), 425-36
CODEN: BRBUDU; ISSN: 0361-9230
DOCUMENT TYPE: Journal
LANGUAGE: English
AB NMR spectroscopy studies of combinations of 5-HT [50-67-9] with tryptophan-contg. peptide sequences and similar peptides from myelin basic protein are given. The binding site appears to consist of the sequence Arg-Phe-Ser-Trp. Similar 5-HT-binding sites exist on LH-RH [33515-09-2] (Tyr-Ser-Trp) and **MSH**-ACTH tetrapeptide [**4289-02-5**] (Phe-Arg-Trp). These binding sites are specific to 5-HT as was demonstrated by lack of binding by other pharmacol. active amines and indoles. Drugs known to affect 5-HT levels, e.g., fenfluramine [458-24-2] and L-DOPA [59-92-7], bound weakly to these sites. Structural and functional similarities between the tryptophan-contg. peptide sequences, LH-RH, and **MSH**-ACTH with an ACTH-like peptide of human leukocyte interferon, human and bovine serum albumin, hen ovalbumin, and with red pigment-concg. hormone [37933-92-9] suggest that the latter

peptides may also contain similar 5-HT-binding sites. The elucidation of 5-HT-binding sites on these peptides and proteins has implications for understanding various aspects of cancer, autoimmunity, neurol. disease, and peptide hormone control.

L18 ANSWER 71 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:192248 HCAPLUS
DOCUMENT NUMBER: 100:192248
TITLE: Protease-catalyzed synthesis of **melanocyte** -stimulating hormone (**MSH**) fragments
AUTHOR(S): Kullmann, Willi
CORPORATE SOURCE: Max-Planck-Inst. Biophys. Chem., Goettingen, Fed. Rep. Ger.
SOURCE: Journal of Protein Chemistry (1983), 2(4), 289-301
CODEN: JPCHD2; ISSN: 0277-8033
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Trypsin, .alpha.-chymotrypsin, papain, carboxypeptidase Y, and thermolysin served as catalysts for the protease-controlled synthesis of some fragments of **MSH**. To obviate proteolytic cleavage of peptide bonds, several expedients leading to the target peptides were developed. The enzymic procedure enabled under mild conditions the prepn. of the desired peptides whose amino acid compn. may cause complications during conventional syntheses.

L18 ANSWER 72 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1983:570003 HCAPLUS
DOCUMENT NUMBER: 99:170003
TITLE: The enhanced recovery of sensorimotor function in rats is related to the melanotropic moiety of ACTH/**MSH** neuropeptides
AUTHOR(S): Bijlsma, Wim A.; Schotman, Peter; Jennekens, Frans G. I.; Gispen, Willem Hendrik; De Wied, David
CORPORATE SOURCE: Inst. Mol. Biol., State Univ. Utrecht, Utrecht, Neth.
SOURCE: European Journal of Pharmacology (1983), 92(3-4), 231-6
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The recovery of sensorimotor function in female rats was studied using a foot-flick response test after crushing the sciatic nerve. Every other day the animals received a s.c. injection of small ACTH/**MSH**-like peptides. Rats treated with ACTH-(4-10) [4037-01-8], ACTH-(4-9) [**56236-83-0**], the ACTH-(4-9) analog ORG 2766 [50913-82-1], ACTH-(6-10) [2279-03-0], and .alpha.-**MSH** [37213-49-3] showed a faster recovery of sensorimotor function than did vehicle-treated rats. Treatment with ACTH-(4-7) [50842-42-7] or Phe7-D-Lys8-Phe9 (the C-terminal part of ORG 2766) [63472-64-0] was ineffective. The effect of .alpha.-**MSH** was stronger than that of the other peptides. The facilitation of the return of sensorimotor function by the ACTH-like peptides is discussed in relation to the corticotropic and melanotropic properties of these peptides. Treatment with ORG 2766 was effective not only in young adult animals (2-3 mo), but also in 1-yr-old animals.

L18 ANSWER 73 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1983:83719 HCAPLUS
DOCUMENT NUMBER: 98:83719
TITLE: Structure-activity relationships of peptides derived from ACTH, .beta.-LPH and **MSH** with regard to

avoidance behavior in rats
AUTHOR(S): Van Nispen, J. W.; Greven, H. M.
CORPORATE SOURCE: Sci. Dev. Group, Organon Int. B.V., Oss, 5340 BH, Neth.
SOURCE: Pharmacology & Therapeutics (1982), 16(1), 67-102
CODEN: PHTHDT; ISSN: 0163-7258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Studies on the structure-activity relations of peptides derived from ACTH, .beta.-lipotropin (.beta.-LPH), and **MSH** on avoidance behavior in rats are described. A no. of nonoverlapping sequences of ACTH and .beta.-LPH are active on extinction of conditioned avoidance behavior in rats in the pole-jumping test. The most important active core in ACTH appears to be in the sequence 4-7. The active core of .beta.-endorphin for the inhibition of extinction appears to be located in the N-terminal portion of the mol.

L18 ANSWER 74 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:437844 HCAPLUS
DOCUMENT NUMBER: 93:37844
TITLE: Effect of various ACTH analogs on lordosis behavior in the female rat
AUTHOR(S): Wilson, C. A.; Thody, A. J.; Everard, D.
CORPORATE SOURCE: Dep. Physiol., R. Vet. Coll., London, NW1 0TU, UK
SOURCE: Hormones and Behavior (1979), 13(3), 293-300
CODEN: HOBEAO; ISSN: 0018-506X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of ACTH [9002-60-2] and various related analogs on lordosis behavior in female rats was compared with that produced by synthetic .alpha.-**MSH** [581-05-5]. Ovariectomized rats received 2 .mu.g estradiol benzoate on Day 1 and Day 3 either 0.1 or 0.2 mg progesterone. Treatment with 20 .mu.g .alpha.-**MSH** on Day 2 stimulated lordosis in nonreceptive rats but inhibited lordosis in the receptive rats. Of the other peptides tested only 4-10-ACTH [4037-01-8] was as effective as .alpha.-**MSH** in facilitating and inhibiting lordosis behavior. 1-24-ACTH [16960-16-0] and 4-9-ACTH [**56236-83-0**] also produced both effects. 1-39-ACTH and 1-16-ACTH [5576-42-1], on the other hand, had neither effect but were both effective in stimulating and inhibiting lordosis when administered on Days 1, 2, and 3. 4-10-ACTH may contain the essential sequence for these facilitatory and inhibitory effects on female **sexual** receptivity and elongation of the peptide chain beyond 1-13-ACTH (.alpha.-**MSH**) may decrease this activity.

L18 ANSWER 75 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1979:433214 HCAPLUS
DOCUMENT NUMBER: 91:33214
TITLE: A quantitative study on the relationship between structure and behavioral activity of peptides related to ACTH
AUTHOR(S): Kelder, J.; Greven, H. M.
CORPORATE SOURCE: Sci. Dev. Group, Organon Int. B. V., Oss, 5340 BH, Neth.
SOURCE: Recueil des Travaux Chimiques des Pays-Bas (1979), 98(4), 168-72
CODEN: RTCPA3; ISSN: 0034-186X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of peptides related to ACTH and **MSH** with behavioral

potencies detd. in a pole-jumping test on rats was analyzed using a modified Free-Wilson method (Fujita-Ban anal.). A stepwise multiple linear regression program was used for the calcn. of the individual contributions of the subunits to the overall activity. Thus, the use of a model based on independent contributions of the amino acid residues in the peptide chain to the overall biolog. activity was justified. Inspection of the few exceptions to this rule led to valuable suggestions about spatial interactions at the receptor level.

L18 ANSWER 76 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1977:439803 HCAPLUS
DOCUMENT NUMBER: 87:39803
TITLE: Des-N.alpha.1-acetyl-.alpha.-melanotropin. A synthetic substrate for specific N-terminal directed enzymic acetylation
AUTHOR(S): Smeets, Paul; Granger, Michele; Van Nispen, Johannes W.; Bloemendal, Hans; Tesser, Godefridus I.
CORPORATE SOURCE: Dep. Org. Chem., Cathol. Univ. Nijmegen, Nijmegen, Neth.
SOURCE: International Journal of Peptide & Protein Research (1977), 9(1), 52-6
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
AB R-Ser-Tyr-Ser-Met-Glu-His-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH2 (I, R = H), deacetyl-**MSH**, was prepd. by coupling BOC-Ser-Tyr-Ser-Met-Glu(OCMe3)-His-Phe-Arg-Trp-OH (BOC = Me3CO2C) to H-Lys(Msc)-Pro-Val-NH2 (II, Msc = MeSO2CH2CH2O2C) with dicyclohexylcarbodiimide and deblocking the resulting protected tridecapeptide amide with CF3CO2H for BOC and CMe3 groups and NaOH for the Msc group. BOC-Lys(Msc)-OC6H4NO2-4 was prepd. and coupled to H-Pro-Val-NH2 to give BOC-Lys(Msc)-Pro-Val-NH2, which was BOC-deblocked with HCl to give II. I (R = H) was selectively acetylated at the N-terminal NH2 by an enzyme system in a cell-free ext. of calf eye lenses to give I (R = Ac) (.alpha.-**MSH**). The latter was prepd., but was not acetylated at the side chain NH2 by the above enzyme system. R1-Ser-Tyr-Ser-Met-Glu(OR2)-His-Phe-Arg-Trp-Gly-Lys(R3)-Pro-Val-NH2 (R1 = R2 = H, R3 = Msc, Ac; R1 = Ac, R2 = H, R3 = Msc, Ac; R1 = BOC, R2 = CMe3, R3 = H, Ac) were also prepd.

L18 ANSWER 77 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:537660 HCAPLUS
DOCUMENT NUMBER: 85:137660
TITLE: Small peptides with **melanocyte**-stimulating activity
AUTHOR(S): Medzihradszky, K.; Medzihradszky-Schweiger, H.
CORPORATE SOURCE: Inst. Org. Chem., Eotvos Lorand Univ., Budapest, Hung.
SOURCE: FEBS Letters (1976), 67(1), 45-7
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In an in vitro frog skin assay, the **melanocyte**-stimulating activities of synthetic .alpha.-**MSH** [581-05-5], Glu-His-Phe-Arg-Trp-Gly-OH [4086-29-7], Ser-Tyr-Ser-Met-OMe [47751-01-9], Glu-His-Phe-OH [60438-42-8], and Arg-Trp-Gly-OMe [4873-87-4] were 4 .times. 1010, 1 .times. 106, 2 .times. 104, 1 .times. 104, and 6 .times. 103 **MSH** units/mmole, resp. Enkephalin fragments exhibited **melanocyte**-stimulating activities similar to the **MSH** tri- and tetrapeptides. Apparently, the Phe-Arg bond does not need to be intact for **melanocyte**-stimulating activity.

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L18 ANSWER 78 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:54380 HCAPLUS
DOCUMENT NUMBER: 84:54380
TITLE: Hormone-receptor interactions. Demonstration of two message sequences (active sites) in .alpha.-melanotropin
AUTHOR(S): Eberle, Alex; Schwyzer, Robert
CORPORATE SOURCE: Inst. Molekularbiol. Biophys., ETH, Zurich, Switz.
SOURCE: Helvetica Chimica Acta (1975), 58(6), 1528-351
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In in vitro structure-activity studies on 21 synthetic peptides related to synthetic .alpha.-**MSH** (I) [581-05-5], the tripeptide amide, H-Lys-Pro-Val-NH2 [57899-80-6], its N.alpha.-acetylderiv. [57899-96-4], and N.alpha.-acetyl-L-lysinamide [19789-60-7] were hormonally active. The results suggest that I has 2 active sites, -Met-Glu-His-Phe-Arg-Trp-Gly-, and -Lys-Pro-Val-NH2 which are capable of independently triggering the hormone receptor responsible for melanin dispersion.

L18 ANSWER 79 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1975:508718 HCAPLUS
DOCUMENT NUMBER: 83:108718
TITLE: Correlation between structure, behavioral activity, and rate of biotransformation of some ACTH4-9 analogs
AUTHOR(S): Witter, Albert; Greven, Henk M.; De Wied, David
CORPORATE SOURCE: Med. Fac., Univ. Utrecht, Utrecht, Neth.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1975), 193(3), 853-60
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of substitutions in ACTH4-9 [**56236-83-0**] on extinction of pole-jumping avoidance behavior in intact rats was investigated systematically at 2-dose levels. Simultaneous introduction of 4-methionine sulfoxide and 8-D-lysine, in combination with 9-phenylalanine, led to a 1000-fold increase in behavioral potency. The same substitutions induced a 1000-fold decrease in a **melanocyte** -stimulating hormone activity. Incubations of 14C-labeled ACTH4-9 analogs, prepd. by reductive methylation, were carried out with plasma and brain exts. The resulting metabolites were sepd. by paper electrophoresis and paper chromatog. The concns. of nonmetabolized hexapeptides, which appeared to be almost entirely responsible for behavioral activity, were detd. as a function of incubation time. The in vitro half-life of intact hexapeptides correlated with their behavioral activity. The in vitro half-life of intact hexapeptides correlated with their behavioral activity. Therefore, the increase in behavioral potency as a result of amino acid substitutions can be explained, at least partly, by increased resistance against biotransformation.

L18 ANSWER 80 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1974:569813 HCAPLUS
DOCUMENT NUMBER: 81:169813
TITLE: Labeled polypeptides. IV. Syntheses of 10-[glycine-1-14C]-.alpha.-melanotropin
AUTHOR(S): Fittkau, Siegfried; Medzihradszky, Kalman; Seproedi, Janos
CORPORATE SOURCE: Physiol.-Chem. Inst., Martin-Luther-Univ., Halle, Ger.

Dem. Rep.
SOURCE: Journal fuer Praktische Chemie (Leipzig) (1974), 316(4), 679-83
CODEN: JPCEAO; ISSN: 0021-8383
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The **melanocyte**-stimulating hormone .alpha.-melanotropin (I) was prep, in 40% yield by fragment condensation of Ac-Ser-Tyr-Ser-Met-N2H3 with Glu(O-CMe3)-His-Phe-Arg-Trp-OMe, lengthening the resulting nonapeptide with Gly-1-14C, coupling the resulting labeled decapeptide with Boc-Lys-Pro-Val-NH2 (Boc = Me3CO2C), and cleaving the protective groups. I had sp. activity 34 mCi/mmole and biol. activity 2 .times. 1010 units/g.

L18 ANSWER 81 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:111999 HCAPLUS
DOCUMENT NUMBER: 70:111999
TITLE: Synthetic approach to studies on the structure-function of **melanocyte**-stimulating hormone
AUTHOR(S): Yajima, Haruaki
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, Japan
SOURCE: Gunma Symposia on Endocrinology (1968), 5, 73-84
CODEN: GUSYAU; ISSN: 0533 6724
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent work on relations between the activity of various synthetic .alpha.- and .beta.-**MSH** and chain-length or stereoisomerism is reviewed. The activity of synthetic .alpha.-**MSH** was 2 .times. 1012 **MSH** units/g. Stereoisomeric pentapeptides, His-Phe-Arg-Trp-Gly, related to the active fragment of **MSH** were synthesized. Histidine and arginine must both be in the L configuration, but replacement of phenylalanine or tryptophan with the D forms increased activity. The results indicated the existence of particular structural requirements for **MSH** activity. All-D-pentapeptide had anti-**MSH** activity at a level of 10-6 times that of melatonin, but attempts to prep. more potent anti-**MSH** peptides proved fruitless. Total synthesis of monkey .beta.-**MSH** was presented and the activity of synthetic intermediates recorded.

L18 ANSWER 82 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1967:2776 HCAPLUS
DOCUMENT NUMBER: 66:2776
TITLE: Histidylphenylalanylarginyltryptophan
PATENT ASSIGNEE(S): Shionogi and Co., Ltd.
SOURCE: Brit., 6 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1037168		19660727		
DE 1470310			DE	
FR 1442330			FR	
FR 4293			FR	
JP 41018506		19660000	JP	

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PRIORITY APPLN. INFO.: JP 19631227

AB (In this abstract BOC = tert-butyloxycarbonyl, Tos = tosyl, Cbzo = benzyloxycarbonyl). All amino acids have the L-configuration). BOC-Phe-Arg-(NG-Tos)- Try-OCH2Ph (I) (2.45 g.) in 7 ml. F3CCO2H left at room-temp. 1 hr. and treated with 100 ml. Et2O gave 2.34 g. Phe-Arg-(NG-Tos)-Try-OCH2Ph trifluoroacetate (II). Shaking 0.886 g. II in 15 ml. AcOEt with 10 ml. 50% aq. K2CO3 at 0.degree. gave 0.86 g. base which was treated in 10 ml. MeCN with 0.423 g. di-Cbzo-histidine followed by 0.206 g. N,N'-dicyclohexylcarbodiimide in 3 ml. MeCN. Filtration of the urea and chromatography of the product (1.15 g.) in 60 g. silica gel gave 0.81 g. di-Cbzo-His-Phe-Arg-(NG-Tos)-Try-OCH2Ph (III), m. 97-105.degree., [.alpha.] 24.5 D -10.9.degree. (c 1.825, MeOH). Treatment of 0.472 g. III in 150 ml. liquid NH3 with Na until the blue color persisted, addn. of 0.2 ml. AcOH, and evapn. of the NH3 gave a residue which was dissolved in 40 ml. 0.1N AcOH, filtered through Celite and absorbed onto an Amberlite CG-50 column. After washing with 700 ml. of 0.25% AcOH and 50 ml. H2O, elution with C5H5NAcOH-H2O (30:4:66) gave 0.306 g. His-Phe-Arg-Try (IV) acetate. Pure IV, [.alpha.] 24.5 D -5.4.degree. (c 0.947, N-HCl) was obtained by chromatography on carboxymethylcellulose and elution with 0.075 MNH4OAc buffer. A reaction scheme is given for the prepn. of I; phys. properties are not quoted. By a similar process from the nitroarginine analog of I is prepd. di-Cbzo-His-Phe-Arg-(NG-NO2)-Try-OCH2Ph (V), m. 167-8.degree. (decompn.), [.alpha.] 24.5 D -12.3.degree. (c 2.08, Me2NCHO). Redn. of 0.5 g. V with Pd and H in 20 ml. of 90% AcOEt gave IV acetate. IV exhibits **melanocyte**-stimulating hormonal activity comparable to that of the known pentapeptide His-Phe-Arg-Try-Gly (Hofmann and Yajima, CA 57, 6523b).

L18 ANSWER 83 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1965:31104 HCAPLUS
DOCUMENT NUMBER: 62:31104
ORIGINAL REFERENCE NO.: 62:5549f,5550a-b
TITLE: Syntheses of peptides related to the N-terminal structure of corticotropin. III. Synthesis of L-histidyl-L-phenylalanyl-L-arginyl-L-tryptophan, the smallest peptide exhibiting the **melanocyte**-stimulating and the lipolytic activities
AUTHOR(S): Otsuka, Hideo; Inouye, Ken
CORPORATE SOURCE: Shionogi Co., Ltd., Osaka
SOURCE: Bulletin of the Chemical Society of Japan (1964), 37(10), 1465-71
CODEN: BCSJA8; ISSN: 0009-2673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB cf. CA 55, 20983c. The title tetrapeptide, corresponding to the amino acid sequence of positions 6-9 in the corticotropin and .alpha.-**MSH** mols., was synthesized and exhibited **MSH** activity of 3.6 .times. 104 units/g. in the in vitro frog skin assay. The compd. also exhibited lipolysis of rabbit perirenal adipose tissue. Thus, the glycine at position 10 was not essential for biol. activity. The NG-tosyl-L-arginine methyl ester synthesis of the tetrapeptide and related compds. is described in detail.

L18 ANSWER 84 OF 84 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1964:61237 HCAPLUS
DOCUMENT NUMBER: 60:61237
ORIGINAL REFERENCE NO.: 60:10785b-e
TITLE: The synthesis of an **MSH** [**melanocyte**-stimulating hormone]- active tetrapeptide,

L-histidyl-L-phenylalanyl-L-arginyl-L-tryptophan

AUTHOR(S): Otsuka, Hideo; Inouye, Ken
CORPORATE SOURCE: Shionogi Co. Ltd., Osaka

SOURCE: Bulletin of the Chemical Society of Japan (1964), 37(2), 289-90
CODEN: BCSJA8; ISSN: 0009-2673
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The title synthetic tetrapeptide (I) exhibited the same level of **MSH** activity as did the pentapeptide, L-His-L-Phe-L-Arg-L-Try-Gly and its D-Phe analog. NG-Tosyl-L-arginine Me ester, m. 98-8.5.degree., [.alpha.]D 14.8.degree. (MeOH), and tert-butoxycarbonyl-L-phenylalanine, prepd. from the dicyclohexylamine salt, m. 210-12.degree. (decompn.), [.alpha.]D 28.9.degree. (MeOH), were condensed by the N,N''dicyclohexylcarbodiimide (DCC) method to give tert-butoxycarbonyl-L-Phe-NG-tosyl-L-Arg Me ester (II), [.alpha.]D -5.9.degree. (MeOH). On sapon. II gave the corresponding amorphous acid, [.alpha.]D 1.0.degree. (MeOH); hydrazide m. 110-14.degree., [.alpha.]D -6.3.degree. (MeOH). The azide derived from the hydrazide was condensed with L-tryptophan benzyl ester, m. 71.degree., [.alpha.]D 12.8.degree. (MeOH), to give a tripeptide, tert-butoxycarbonyl-L-Phe-NG-tosyl-L-Arg-L-Try benzyl ester, [.alpha.]D -6.6.degree. (MeOH). The tert-butoxycarbonyl group of the tripeptide was removed with CF3CO2H and the product condensed with N.alpha.,NIm-dicarbobenzoxy-L-histidine by the DCC method to give the tetrapeptide, N.alpha.,NIm-dicarbobenzoxy-L-His-L-Phe-NG-tosyl-L-Arg-L-Try benzyl ester, [.alpha.]D -10.9.degree. (MeOH). Removal of protective groups with Na in liquid NH3 gave I, homogeneous on paper chromatography, Rf 0.55 in 4:1:2 BuOH-HOAc-H2O, and on paper electrophoresis at pH 3.8,6.6, and 11.1, [.alpha.]D -5.4.degree. (N HCl). The **MSH** activity of I was 3.6 .times. 104 units/g.